

SEARCH REQUEST FORM

116584

Requestor's Name: Irene Marx Serial Number: 10/077223

Date: 3/11/04 Phone: 20919 Art Unit: 1651

3E71

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

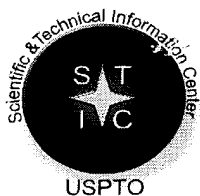
Please search
- Inventions
(claims 1-3, 819 elected)
- composition of 20 or more Krebs cycle
(citric acid cycle) intermediates
- 2 or more compounds of cl. 3.
- cl 3 products, + products of cl. 8
- composition as tablet, injection,
infusion, inhalant, suppository, etc.

STAFF USE ONLY

Date completed: 3/14/04
Searcher: u
Terminal time: _____
Elapsed time: 10 + 100
CPU time: _____
Total time: _____
Number of Searches: _____
Number of Databases: _____

Search Site
☒ STIC
☐ CM-1
☐ Pre-S
Type of Search
☐ N.A. Sequence
☐ A.A. Sequence
☐ Structure
☒ Bibliographic

Vendors
☐ IG
☒ STN
☐ Dialog
☐ APS
☐ Geninfo
☐ SDC
☐ DARC/Questel
☐ Other



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 116686

TO: Irene Marx
Location: 3a79
Sunday, March 14, 2004
Art Unit: 1651
Phone: 272-0919
Serial Number: 10 / 077283

3E71

From: Jan Delaval
Location: Biotech-Chem Library
Rem 1A51
Phone: 272-2504

jan.delaval@uspto.gov

Search Notes

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 10:59:31 ON 14 MAR 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 14 Mar 2004 VOL 140 ISS 12

FILE LAST UPDATED: 12 Mar 2004 (20040312/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 09:24:04 ON 14 MAR 2004)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 09:27:01 ON 14 MAR 2004

E RATH M/AU
L1 84 S E15-E17,E3-E7
L2 20 S L1 AND P/DT
E KREBS/CT
E E7+ALL
E E2+ALL
L3 4758 S E3
L4 11174 S E3-E8/BI
L5 339 S CIS ACONITATE
L6 272 S CIS ACONITIC ACID
L7 357 S CIS(L)ACONITIC ACID
L8 126392 S CITRIC ACID OR CITRATE
L9 9135 S ISOCITRATE OR ISOCITRIC ACID
L10 23 S OXALSUCCINATE OR OXALSUCCINIC ACID
L11 148 S OXALSUCCINATE OR OXALOSUCCINATE OR (OXALSUCCINIC OR OXALOSUCC
L12 10044 S (ALPHA OR ALFA) () (KETOGLUTARATE OR KETO GLUTARATE OR (KETOGLU
L13 267 S SUCCINYL () (COE OR COENZYME OR CO ENZYME) () A
L14 10 S SUCCINATE () (COE OR COENZYME OR CO ENZYME) () A
L15 477 S (SUCCINATE OR SUCCINYL) (L) (COE OR COENZYME OR CO ENZYME) () A
L16 72540 S SUCCINATE OR SUCCINIC ACID
L17 29738 S FUMARATE OR FUMARIC ACID
L18 2877 S L () (MALATE OR MALIC ACID)
L19 7367 S OXALACETATE OR OXALACETIC ACID
L20 1835 S ACETYL () (COE OR COENZYME OR CO ENZYME) () A
L21 9566 S ACETYL COA
L22 1140 S (SUCCINYL OR SUCCINATE) () COA
L23 60484 S PYRUVATE OR PYRUVIC ACID

FILE 'REGISTRY' ENTERED AT 09:51:06 ON 14 MAR 2004

L24 12 S 110-15-6 OR 77-92-9 OR 585-84-2 OR 320-77-4 OR 1948-82-9 OR 3
L25 44084 S (110-15-6 OR 77-92-9 OR 585-84-2 OR 320-77-4 OR 1948-82-9 OR
L26 32099 S L25 NOT ((PMS OR CCS OR AYS OR MNS OR MXS OR IDS)/CI OR COMPD
L27 32083 S L26 NOT SQL/FA

L28 2 S L24 AND NR>=1
L29 9 S L27 AND (604-98-8 OR 72-89-9)/CRN
L30 30372 S L27 AND NR>=1
L31 1711 S L27 NOT L30
L32 1720 S L29,L31

FILE 'HCAPLUS' ENTERED AT 09:54:20 ON 14 MAR 2004

L33 114420 S L24 OR L32
L34 298526 S L3-L23,L33
L35 2987 S LIPOIC ACID
L36 1254 S LIPOAMIDE
L37 0 S ACETYLLIPOAMIDE OR ACETYLIPOAMIDE OR ACETYL LIPOAMIDE
L38 0 S LIPOAMIDE() (ACETYL OR ACETATE)
L39 16 S LIPOAMIDE(S) (ACETYL OR ACETATE OR ACETIC ACID)
L40 3 S L36(L)DIACET?
L41 0 S DIACETYLLIPOAMIDE
L42 1 S DIACETYL LIPOAMIDE
L43 93776 S LYSINE
L44 8921 S CARNITINE
L45 85808 S ASCORBATE OR ASCORBIC ACID
L46 20046 S THIAMINE
L47 12222 S RIBOFLAVIN
L48 19052 S NICOTINIC ACID
L49 920 S NIACINAMIDE
L50 8658 S PANTOTHENATE OR PANTOTHENIC ACID
L51 5835 S NICOTINAMIDE ADENINE DINUCLEOTIDE
L52 2268 S REDUCED NICOTINAMIDE ADENINE DINUCLEOTIDE
L53 2221 S NICOTINAMIDE ADENINE DINUCLEOTIDE PHOSPHATE
L54 925 S REDUCED NICOTINAMIDE ADENINE DINUCLEOTIDE PHOSPHATE
L55 2578 S QUINOLINATE OR QUINOLINIC ACID
L56 8784 S FLAVIN ADENINE DINUCLEOTIDE
L57 3 S REDUCED FLAVIN ADENINE DINUCLEOTIDE
L58 12 S REDUCED FLAVIN MONONUCLEOTIDE
L59 3297 S ADENOSINE DIPHOSPHATE
L60 13839 S ADENOSINE TRIPHOSPHATE
L61 496 S GUANOSINE DIPHOSPHATE
L62 1560 S GUANOSINE TRIPHOSPHATE
L63 39884 S (MG OR MAGNESIUM OR CA OR CALCIUM OR MN OR MANGANESE)() ION
L64 38 S (CU OR COPPER)() (FE OR IRON)() (SULFATE OR SULPHATE OR SO4)
L65 10486 S (CU OR COPPER OR CUPR?) (L) (FE OR FE2 OR FERRIC OR FERROUS OR
L66 562296 S MOLYBDENUM OR MO

FILE 'REGISTRY' ENTERED AT 10:19:04 ON 14 MAR 2004

L67 22 S 89-00-4 OR 146-14-5 OR 146-17-8 OR 5666-16-0 OR 58-64-0 OR 56
L68 23 S 89-00-9 OR 146-14-5 OR 146-17-8 OR 5666-16-0 OR 58-64-0 OR 56
L69 8 S 62624-30-0 OR 10504-35-5 OR 37138-77-5 OR 53-84-9 OR 53-59-8
L70 2 S 10028-22-5 OR 7758-98-7
L71 22612 S 7664-93-9/CRN
L72 396 S L71 AND CU/ELS
L73 430 S L71 AND FE/ELS
L74 29 S L72 AND L73
L75 14 S L74 NOT AYS/CI
L76 5 S L75 NOT MXS/CI
L77 2 S L76 NOT (GRAPHITE OR MNS/CI)
L78 522 S L72,L73 NOT (AYS OR MXS OR MNS OR CCS)/CI
L79 81 S L78 AND 2/NC
L80 21 S L79 AND SALT
L81 18 S L80 NOT (59FE OR 55FE OR N/ELS)
L82 31 S L67-L69
SEL RN
L83 5357 S E1-E31/CRN
L84 852 S L83 NOT ((AYS OR PMS OR MXS OR MNS OR CCS OR IDS)/CI OR COMPD
L85 903 S L70,L77,L81,L82,L84

L86 418 S (MG OR CA OR MN OR MO)/MF
L87 115 S L86 NOT ISOTOPE
L88 1018 S L85,L87

FILE 'HCAPLUS' ENTERED AT 10:28:29 ON 14 MAR 2004

L89 943555 S L88

FILE 'REGISTRY' ENTERED AT 10:28:59 ON 14 MAR 2004

L90 1 S 940-69-2
L91 773 S S2C3/ES AND 1/NR AND (O AND N)/ELS
L92 111 S L91 AND ACET
L93 55 S L92 AND 1/NC
L94 35 S L93 NOT CCS/CI
L95 56 S L92 NOT L93
L96 33 S L95 NOT MXS/CI
L97 11 S L96 NOT RU/ELS
L98 4 S 940-69-2/CRN
L99 731 S L91 NOT RU/ELS
L100 666 S L99 NOT MXS/CI
L101 664 S L100 NOT CCS/CI
L102 70 S L101 AND ?ACET?/CNS
L103 47 S L102 AND 2/S
L104 23 S L103 AND 1/N
L105 1 S L104 AND C10H17NO2S2
L106 0 S 214554-83-3/CRN

FILE 'HCAPLUS' ENTERED AT 10:34:27 ON 14 MAR 2004

L107 2 S L105
L108 943555 S L89,L107
L109 52269 S L35-L66,L108 AND L34
L110 4 S L1 AND L109
L111 52423 S L34 AND (L35-L66,L108 OR ASCORB?)
L112 52423 S L109,L111
L113 4 S L1 AND L112
L114 4 S L110,L113
L115 2405 S L112 AND (L24 OR L32) (L) (THU OR BAC OR DMA OR PAC OR PKT)/RL
L116 1860 S L115 AND (L88 OR L105) (L) (THU OR BAC OR DMA OR PAC OR PKT)/R
L117 1249 S L116 AND (PHARMACEUT? OR PHARMACOL?)/SC,SX
L118 674 S L117 AND COMPOSITION
L119 683 S L117 AND (COMBIN? OR MIX? OR SYNERG? OR FORMUL?)
L120 972 S L118,L119
L121 761 S L120 AND (PD<=20010214 OR PRD<=20010214 OR AD<=20010214)
L122 1 S L121 AND (BIOENERG? OR BIO(L) ENERG?)
L123 5 S L114,L122
E RATH/PA,CS
L124 4 S E24-E30
L125 3 S L124 NOT RATH/TI
L126 7 S L123,L125
E ENERGY/CT
L127 4 S L121 AND ENERGY/CW
E ENERGY METABOLISM/CT
E E4+ALL
L128 7453 S E3,E2
E E7+ALL
L129 1653 S E1
L130 675742 S E3+NT
L131 199805 S E7+NT
L132 21 S L121 AND L128-L131
L133 29 S L126,L127,L132
L134 22 S L133 NOT L126
E UREA CYCLE/CT
E E3+ALL
L135 627 S E2

L136 1 S L135 AND L121
E METABOLISM/CT
E E13+ALL
L137 19 S E2,E1+NT AND L121
E METABOLISM/CT
E E3+ALL
L138 15 S E1+NT AND L121
L139 25 S L137,L138
L140 21 S L139 NOT L133
SEL DN AN 1 3 12 13 17 18
L141 6 S E1-E16
L142 13 S L126,L141
L143 13 S L142 AND L1-L23,L33-L66,L89,L107-L142
L144 10 S L143 AND (KREB OR ?SUCCIN? OR ?FUMAR? OR ?MALIC? OR ?MALATE?
L145 13 S L143,L144

FILE 'HCAPLUS' ENTERED AT 10:59:31 ON 14 MAR 2004

=> d all hitstr tot l145

L145 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:182238 HCAPLUS
ED Entered STN: 05 Mar 2004
TI Metabolic uncoupling therapy
IN McCleary, Edward Larry
PA USA
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 749,584.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-7076
ICS A61K031-685; A61K031-525; A61K031-195; A61K031-198
NCL 424094100; 514046000; 514251000; 514078000; 514356000; 514393000;
514561000; 514350000; 514565000; 514250000
CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 18
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004043013	A1	20040304	US 2003-462958	20030617 <--
	US 2002132219	A1	20020919	US 2000-749584	20001228 <--
	US 6579866	B2	20030617		
PRAI	US 2000-749584	A2	20001228	<--	

AB A **combination** of chemical agents reduces reductive stress by limiting the accumulation of high-energy electrons potentially available to the electron transport chain. A method of metabolic uncoupling therapy (MUT) comprises: analyzing a specific physiol. process involving reductive stress; identifying a plurality of MUT agents that modulate metabolic pathways by influencing electron flux; and **formulating a combination** of MUT agents that limits the accumulation of high-energy electrons potentially available to the electron transport chain.

ST metabolic uncoupling therapy electron transport vitamin
IT Amino acids

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(branched; metabolic uncoupling therapy)

IT **Metabolism, animal**

(high-energy electrons in; metabolic uncoupling therapy)

IT Antibiotics

Electron transport system, biological

Metabolic pathways

(metabolic uncoupling therapy)

IT Vitamins
 RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (metabolic uncoupling therapy)

IT Albumins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (metabolic uncoupling therapy)

IT Phosphatidylcholines
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (metabolic uncoupling therapy)

IT Sphingomyelins
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (metabolic uncoupling therapy)

IT Phenols
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (polyphenols, nonpolymeric; metabolic uncoupling therapy)

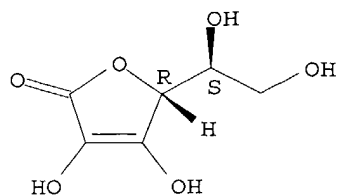
IT Drug interactions
 (synergistic; metabolic uncoupling therapy)

IT 50-69-1, Ribose **50-81-7**, vitamin C 50-99-7, Glucose 51-84-3, Acetylcholine 54-47-7, Pyridoxal phosphate 56-40-6, Glycine 56-41-7, L-Alanine 56-45-1, L-Serine 56-84-8, Aspartic acid 56-85-9, Glutamine 57-00-1, Creatine 58-85-5, Biotin 59-30-3 **59-43-8**, vitamin B1 62-49-7, Choline 65-23-6, Pyridoxine 68-19-9, vitamin B12 70-51-9 74-79-3, Arginine **79-83-4**, vitamin B3 **83-88-5**, **Riboflavin** 87-89-8, (myo)Inositol **98-92-0**, vitamin B3 107-35-7, Taurine 107-43-7, Trimethylglycine **127-17-3 144-23-0**, Magnesium **citrate** 144-55-8, Carbonic acid monosodium salt 303-98-0, coenzyme Q10 **541-15-1**, **Carnitine** 541-50-4 563-24-6 1406-16-2, vitamin D 1406-18-4, vitamin E 3040-38-8, Acetyl-L-**carnitine**) 6829-55-6D, Tocotrienol, analogs **7439-95-4**, Magnesium 7440-09-7, Potassium 7440-47-3, Chromium **7440-70-2**, Calcium 7647-14-5, Sodium chloride 7782-49-2, Selenium 8059-24-3, vitamin B6 9004-10-8, Insulin 17298-37-2, Propionyl **carnitine** 27750-10-3, **Hydroxycitric** acid 27774-13-6, Vanadyl sulfate 29908-03-0 32839-18-2 32839-30-8 57828-26-9, **Lipoic acid** 102518-79-6, Huperzine A
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (metabolic uncoupling therapy)

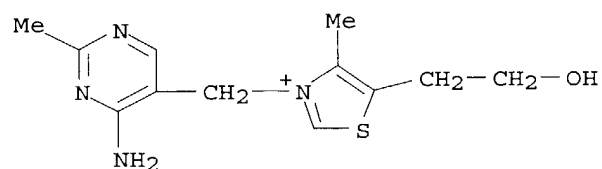
IT **50-81-7**, vitamin C **59-43-8**, vitamin B1 **79-83-4**, vitamin B3 **83-88-5**, **Riboflavin** **98-92-0**, vitamin B3 **127-17-3 144-23-0**, Magnesium **citrate** **541-15-1**, **Carnitine** **7439-95-4**, Magnesium **7440-70-2**, Calcium
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (metabolic uncoupling therapy)

RN 50-81-7 HCAPLUS
 CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



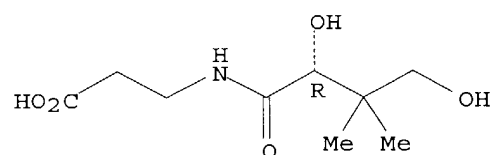
RN 59-43-8 HCAPLUS
 CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-
 4-methyl- chloride (9CI) (CA INDEX NAME)



● Cl⁻

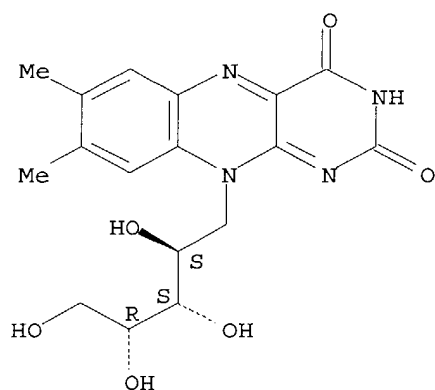
RN 79-83-4 HCAPLUS
 CN β-Alanine, N-[(2R)-2,4-dihydroxy-3,3-dimethyl-1-oxobutyl]- (9CI) (CA
 INDEX NAME)

Absolute stereochemistry. Rotation (+).

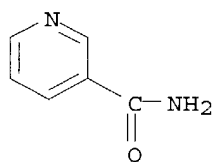


RN 83-88-5 HCAPLUS
 CN Riboflavin (8CI, 9CI) (CA INDEX NAME)

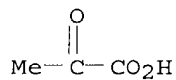
Absolute stereochemistry.



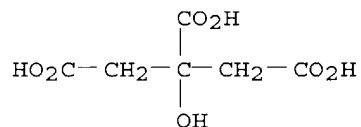
RN 98-92-0 HCAPLUS
 CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)



RN 127-17-3 HCAPLUS
 CN Propanoic acid, 2-oxo- (9CI) (CA INDEX NAME)



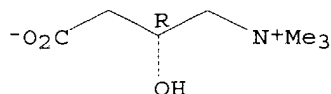
RN 144-23-0 HCAPLUS
 CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, magnesium salt (1:1) (9CI)
 (CA INDEX NAME)



● Mg

RN 541-15-1 HCAPLUS
 CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 7439-95-4 HCAPLUS
 CN Magnesium (8CI, 9CI) (CA INDEX NAME)

Mg

RN 7440-70-2 HCAPLUS
 CN Calcium (8CI, 9CI) (CA INDEX NAME)

Ca

L145 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:173419 HCAPLUS
 DN 138:221848
 ED Entered STN: 07 Mar 2003
 TI Preparation of novel **ascorbic acid lysine**
 and proline derivatives
 IN Roomi, Waheed; Netke, Shrirang; Ivanov, Vadim; Niedzwiecki, Aleksandra
 PA **Rath, Matthias, USA**
 SO PCT Int. Appl., 41 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-34
 ICS C07D305-12
 CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 33, 62

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018000	A1	20030306	WO 2002-US27060	20020823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003119753	A1	20030626	US 2002-226588	20020823

PRAI US 2001-314857P P 20010824

AB **L-Ascorbic acid** esters with **lysine** or **lysine** moieties or proline or proline moieties were prepared for use in compns. used to prevent the degradation of extracellular matrix, stabilize connective tissue, as antioxidants, and for treating damage to skin. Thus, treating 8 mmol **L-ascorbic acid** with 10 mmol **L-lysine** in 20 mL sulfuric acid overnight at room temperature afforded **L-ascorbyl-6-lysine**.

ST **ascorbic acid** ester **lysine** proline prepn

dermatol application

IT Amino acids, preparation
 RL: COS (Cosmetic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (ascorbate esters; preparation of novel **ascorbic acid** lysinate or proline derivs.)

IT Antioxidants
 Connective tissue
 Extracellular matrix
 (preparation of novel **ascorbic acid** lysinate or proline derivs.)

IT 25213-33-6DP, Poly[(2S)-1,2-pyrrolidinediylcarbonyl], reaction products with 6-deoxybromo **ascorbate** or 6-deoxyamino **ascorbate**
 38000-06-5DP, reaction products with 6-deoxybromo **ascorbate** or 6-deoxyamino **ascorbate** 62983-44-2DP, reaction products with polylysine or polyproline 85366-70-7DP, reaction products with polylysine or polyproline 498576-94-6P 498576-96-8P 500893-69-6P
 500893-70-9P 500893-71-0P 500893-72-1P 500893-73-2P 500893-74-3P
 500893-75-4P 500893-76-5P 500893-77-6DP, reaction products with polylysine 500893-78-7DP, reaction products with polyproline
 500893-79-8P 500893-80-1P 500893-81-2P 500893-82-3P 500893-83-4P
 500893-84-5P 500893-85-6P 500893-86-7P 500893-87-8P 500893-88-9P
 500893-89-0P 500893-90-3P 500893-91-4P 500893-92-5P 500893-93-6P
 500893-94-7P 500893-95-8P 500893-96-9P 500893-97-0P 500893-98-1P
 500893-99-2P 500894-00-8P 500894-02-0P 500894-03-1P 500894-04-2P
 500894-05-3P 500894-06-4P 500903-96-8P 500903-97-9P 500903-98-0P
 500903-99-1P 500904-02-9P 500904-05-2P 500904-06-3P 500904-07-4P
 500904-08-5P 500904-09-6P 500904-10-9P
 RL: COS (Cosmetic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of novel **ascorbic acid** lysinate or proline derivs.)

IT 50-81-7, **Ascorbic acid**, reactions
 56-87-1, L **Lysine**, reactions 147-85-3, L Proline, reactions 15042-01-0, 5 6 Isopropylidene **ascorbic acid**
 62983-44-2 85366-70-7 175446-63-6 500894-01-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of novel **ascorbic acid** lysinate or proline derivs.)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

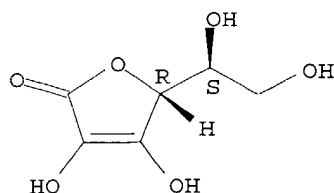
RE (1) Khaled; US 5977073 A 1999 HCAPLUS

IT 50-81-7, **Ascorbic acid**, reactions
 56-87-1, L **Lysine**, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of novel **ascorbic acid** lysinate or proline derivs.)

RN 50-81-7 HCAPLUS

CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

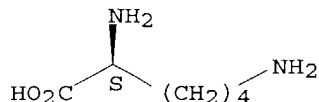
Absolute stereochemistry.



RN 56-87-1 HCAPLUS

CN L-Lysine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L145 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:169981 HCAPLUS

DN 138:180774

ED Entered STN: 06 Mar 2003

TI **Compositions** of flavonoids and **synergists** for use as cytoprotectants and methods of making and using them

IN Brown, Lesley A.; Miller, Guy

PA Galileo Laboratories, Inc., USA

SO U.S., 28 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K007-42

NCL 424059000; 424401000; 514456000; 514045000; 514046000; 514047000; 514048000; 514028000; 536026700; 536027600

CC 1-12 (**Pharmacology**)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6528042	B1	20030304	US 2000-684607	20001006 <--
PRAI	US 1999-159003P	P	19991008	<--	

AB Non-naturally-occurring **compns.** for use in amelioration of disruption of energy metabolism secondary to stress are described. These **compns.** comprise a flavonoid or derivative thereof and a **synergist**. **Synergists** include, but are not limited to, amino acids, carbohydrates, **carnitines**, flavonoids, nucleosides, and tocopherols and/or derivs. thereof. Methods of making these **compns.** and methods of ameliorating disruption of energy metabolism secondary to stress, comprising administering such **synergistic compns.**, are also disclosed.

ST flavonoid **synergist combination** cytoprotectant energy metab stress; amino acid flavonoid **combination** cytoprotectant energy metab stress; carbohydrate flavonoid **combination** cytoprotectant energy metab stress; **carnitine** flavonoid **combination** cytoprotectant energy metab stress; nucleoside flavonoid **combination** cytoprotectant energy metab stress; tocopherol flavonoid **combination** cytoprotectant energy metab stress

IT Animal cell line
(GCL1; flavonoid-**synergist combination composition** for cytoprotectant)

IT Animal tissue culture
(chemical insult; flavonoid-**synergist combination composition** for cytoprotectant)

IT Nucleosides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs.; flavonoid-**synergist combination composition** for cytoprotectant)

IT Toxicity
(drug, stress from; flavonoid-**synergist combination**)

- composition for cytoprotectant)
- IT **Metabolism**
(energy; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Aging, animal
Cytoprotective agents
Cytotoxicity
Exercise
Stress, animal
(flavonoid-**synergist combination composition** for cytoprotectant)
- IT Amino acids, biological studies
Carbohydrates, biological studies
Flavonoids
Nucleosides, biological studies
Tocopherols
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(flavonoid-**synergist combination composition** for cytoprotectant)
- IT Nutrition, animal
(nutritional **composition**; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Cell death
(reduction; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Chemicals
(stress from chemical insult; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Environment
(stress from environmental alteration; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Toxins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(stress from exposure to; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Physiology, animal
(stress from phsysiol. condition; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Surgery
(stress from pre-surgical preparation or post-surgical conditions; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Chemotherapy
Fever and Hyperthermia
Hypothermia
Hypoxia, animal
Ionizing radiation
(stress from; flavonoid-**synergist combination composition** for cytoprotectant)
- IT Drug interactions
(**synergistic**; flavonoid-**synergist combination composition** for cytoprotectant)
- IT 56-40-6, Glycine, biological studies 56-41-7, L-Alanine, biological studies 58-61-7, Adenosine, biological studies 58-63-9, Inosine 59-02-9, α -Tocopherol 59-23-4, Galactose, biological studies 117-39-5, Quercetin 119-13-1, (+)- δ -Tocopherol 127-17-3, biological studies 153-18-4, Rutin 480-40-0, Chrysin 486-66-8, Daidzein 488-69-7, Fructose-1,6-bisphosphate 491-70-3, Luteolin 491-80-5, Biochanin A 520-26-3, Hesperidin 520-27-4, Diosmin 520-33-2, Hesperetin 541-15-1, **Carnitine** 541-15-1D, **Carnitine**, derivs. 616-91-1, N-Acetylcysteine 3040-38-8, Acetylcarnitine 5556-48-9, Ribulose

7616-22-0, γ -Tocopherol 20762-30-5, ADP-ribose 35054-79-6,
Hydroxybutyric acid 36687-82-8, biological studies

RL: **PAC (Pharmacological activity); THU (Therapeutic
use); BIOL (Biological study); USES (Uses)**

(flavonoid-synergist combination composition
for cytoprotectant)

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

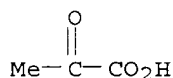
- (1) Amiel, M; Ann Cardiol Angeiol 1998, V47(3), P185 MEDLINE
 - (2) Arora, A; Arch Biochem Biophys 1998, V356(2), P133 HCAPLUS
 - (3) Bahl, J; Ann Rev Pharmacol Toxicol 1987, V27, P257 HCAPLUS
 - (4) Bernier, M; Free Radic Biol Med 1991, V10, P287 HCAPLUS
 - (5) Bidet; US 5849786 A 1998 HCAPLUS
 - (6) Bierber, L; Ann Rev Biochem 1988, V57, P261
 - (7) Bombardelli; US 5043323 A 1991 HCAPLUS
 - (8) Bonnefont-Rousselot, D; Radiat Res 1999, V151, P343 HCAPLUS
 - (9) Bouskela, E; Int J Microcirc 1995, V15(suppl 1), P22
 - (10) Boveris, A; Biochem J 1973, V134, P707 HCAPLUS
 - (11) Ciolino, H; Cancer Res 1998, V58, P2754 HCAPLUS
 - (12) Clarkson; US 5952374 A 1999 HCAPLUS
 - (13) Crandall; US 5945409 A 1999 HCAPLUS
 - (14) Delbarre, B; Int J Microcirc 1995, V15(suppl 1), P27
 - (15) Dumon, M; Ann Biol Clin 1994, V52, P265 HCAPLUS
 - (16) Freneix-Clerc, M; Ann Biol Clin 1994, V52, P171 HCAPLUS
 - (17) Friesenecker, B; Int J Microcirc Clin Exp 1995, V15(suppl 1), P17
 - (18) Gebicki, S; Biochem J 1999, V338, P629 HCAPLUS
 - (19) Goa, K; Drugs 1987, V34, P1 MEDLINE
 - (20) Gorbach; US 5733926 A 1998 HCAPLUS
 - (21) Guidot, D; J Clin Invest 1995, V96, P1131 HCAPLUS
 - (22) Guillot, R; Pancreas 1998, V17(3), P301 MEDLINE
 - (23) Hermes-Lima, M; Mol Cell Biochem 1995, V145, P53 HCAPLUS
 - (24) Hodgson, J; Atherosclerosis 1999, V145, P167 HCAPLUS
 - (25) Jenkinson, S; Clin Chest Med 1989, V10(1), P37 MEDLINE
 - (26) Kowaltowski, A; Am J Physiol 1995, V269, P141 HCAPLUS
 - (27) Kowaltowski, A; FEBS Letters 1998, V425, P213 HCAPLUS
 - (28) Kowaltowski, A; J Biol Chem 1996, V271(6), P2929 HCAPLUS
 - (29) Kubo, K; Br J Nutr 1997, V78, P655 HCAPLUS
 - (30) Kuppusamy, U; Planta Med 1993, V59, P508 HCAPLUS
 - (31) Langley, S; Comp Biochem Physiol 1992, V103A(4), P793 HCAPLUS
 - (32) Lanzendorfer; US 5952373 A 1999 HCAPLUS
 - (33) Matsugo, S; Biochem Biophys Res Comm 1997, V240, P819 HCAPLUS
 - (34) Melzig, M; Pharmazie 1999, V54, P298 HCAPLUS
 - (35) Miller; US 5801159 A 1998 HCAPLUS
 - (36) Minotti, G; Free Radic Biol Med 1987, V3, P379 HCAPLUS
 - (37) Nolte, D; Int J Microcirc 1997, V17(suppl 1), P6
 - (38) Rebouche, C; Ann Rev Nutr 1986, V6, P41 HCAPLUS
 - (39) Reiter, R; Ann N Y Acad Sci 1998, V854, P410 HCAPLUS
 - (40) Saija, A; Free Radic, Biol Med 1995, V19(4), P481 HCAPLUS
 - (41) Saini, T; Res Comm Mol Pathol Pharmacol 1998, V101(3), P259 HCAPLUS
 - (42) Shu-Sen, L; Biosc Rep 1997, V17(3), P259
 - (43) Singh; US 5858371 A 1999 HCAPLUS
 - (44) So, F; Cancer Lett 1997, V112, P127 HCAPLUS
 - (45) Sole; US 6080788 A 2000 HCAPLUS
 - (46) Suzuki, H; Biochem Biophys Res Commun 1998, V249, P542 HCAPLUS
 - (47) Tangeras, A; Biochim Biophys Acta 1980, V589, P162 MEDLINE
 - (48) Teel, R; Cancer Lett 1998, V133, P135 HCAPLUS
 - (49) Toda, S; Phytother Res 1999, V13, P163 HCAPLUS
 - (50) Turrens, J; Bioscience Reports 1997, V17(1), P3 HCAPLUS
 - (51) Unruh, H; Chest Surg Clin N Am 1995, V5(1), P91 MEDLINE
 - (52) Warren; US 5587176 A 1996 HCAPLUS
 - (53) Watabe, S; Eur J Biochem 1997, V149, P52
 - (54) Zhao; J Neurosci Res 1996, V45, P282 HCAPLUS
- IT 127-17-3, biological studies 541-15-1, Carnitine

541-15-1D, Carnitine, derivs.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(flavonoid-synergist combination composition for cytoprotectant)

RN 127-17-3 HCAPLUS

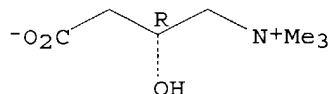
CN Propanoic acid, 2-oxo- (9CI) (CA INDEX NAME)



RN 541-15-1 HCAPLUS

CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)- (9CI) (CA INDEX NAME)

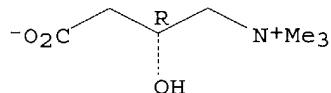
Absolute stereochemistry. Rotation (-).



RN 541-15-1 HCAPLUS

CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L145 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:5244 HCAPLUS

DN 138:49962

ED Entered STN: 03 Jan 2003

TI **Composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells

IN **Rath, Matthias**

PA USA

SO U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO

DT **Patent**

LA English

IC ICM A61K033-06

ICS A61K031-375; A61K031-198

NCL 424682000; 514474000; 514565000

CC 1-12 (**Pharmacology**)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003003162	A1	20030102	US 2001-885347	20010619
	US 6686340	B2	20040203		
PRAI	US 2001-885347		20010619		
AB	The invention relates to a method of administering to a human subject a				

- composition** comprising a vitamin, an amino acid and a trace element for the prevention and treatment of health conditions caused by constriction of smooth muscle cells in organs of the human body like high blood pressure, asthma, glaucoma and tinnitus. The **composition** comprises a vitamin such as **ascorbic acid**, an amino acid such as arginine, and a trace element such as magnesium.
- ST smooth muscle constriction disorder vitamin amino acid trace element;
asthma tinnitus hypertension vitamin amino acid trace element therapy
- IT Heart, disease
(angina pectoris; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Flavonoids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(citrus; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Asthma
Glaucoma (disease)
Human
Hypertension
Muscle contraction
(**composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Amino acids, biological studies
Carotenes, biological studies
Trace elements, biological studies
Vitamins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Fertility
(disorder; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Sexual behavior
(impotence; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Drug delivery systems
(infusions; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Drug delivery systems
(inhalants; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Drug delivery systems
(injections; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Lung, disease
(obstructive; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Ovarian cycle
(premenstrual syndrome; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Muscle
(smooth; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Muscle, disease
(spasm, of ureter, urethra, stomach, gall duct; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)
- IT Drug delivery systems
(suppositories; **composition** and method for prevention and

treatment of health conditions caused by constriction of smooth muscle cells)

IT Drug delivery systems
(tablets; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)

IT Ear, disease
(tinnitus; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)

IT Tocopherols
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β , γ , δ **mix**; **composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)

IT 7439-96-5D, Manganese, chelates 7440-09-7D, Potassium, chelates
RL: PAC (Pharmacological activity); BIOL (Biological study)
(**composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)

IT 50-81-7, L-Ascorbic acid, biological studies
52-90-4, L-Cysteine, biological studies 56-40-6D, Glycine, chromium complexes 56-40-6D, Glycine, molybdenum complexes
56-87-1, L-Lysine, biological studies 58-85-5, Biotin
59-02-9, D- α -Tocopherol 59-30-3, Folic Acid, biological studies
59-43-8, Thiamine, biological studies 59-67-6, Niacin, biological studies 65-23-6, Pyridoxine 67-97-0, Cholecalciferol 68-19-9, Cyanocobalamin 74-79-3, Arginine, biological studies 83-88-5, Riboflavin, biological studies
87-89-8, Inositol 98-92-0, Niacinamide 127-40-2, Lutein 137-08-6 137-66-6, Ascorbyl Palmitate
144-23-0, Magnesium Citrate 147-85-3, L-Proline, biological studies 303-98-0, Coenzyme Q10 432-70-2, α -Carotene 472-70-8, Kryptoxanthin 541-15-1, L-Carnitine
3211-76-5, L-Selenomethionine 5743-27-1, Calcium Ascorbate 7235-40-7, β -Carotene 7439-95-4, Magnesium, biological studies 7439-98-7D, Molybdenum, complexes with glycine 7440-47-3D, Chromium, complexes with glycine 7693-13-2, Calcium Citrate 7757-93-9, Dicalcium Phosphate 13479-54-4, Copper Glycinate 14281-83-5, Zinc Glycinate 14783-68-7 15431-40-0, Magnesium Ascorbate
15595-35-4, Arginine hydrochloride 35947-07-0, Calcium Glycinate 72746-33-9, ζ -Carotene 174882-69-0, Pycnogenol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)

IT 7439-96-5D, Manganese, chelates
RL: PAC (Pharmacological activity); BIOL (Biological study)
(**composition** and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)

RN 7439-96-5 HCAPLUS
CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

IT 50-81-7, L-Ascorbic acid, biological studies
56-87-1, L-Lysine, biological studies 59-43-8, Thiamine, biological studies 59-67-6, Niacin, biological studies 83-88-5, Riboflavin, biological studies
98-92-0, Niacinamide 137-08-6 144-23-0, Magnesium Citrate 541-15-1, L-Carnitine
5743-27-1, Calcium Ascorbate 7439-95-4,

Magnesium, biological studies 7439-98-7D, Molybdenum, complexes with glycine 7693-13-2, Calcium Citrate 15431-40-0, Magnesium Ascorbate

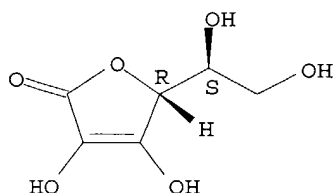
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(composition and method for prevention and treatment of health conditions caused by constriction of smooth muscle cells)

RN 50-81-7 HCAPLUS

CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

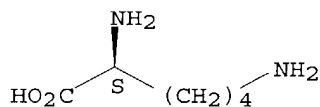
Absolute stereochemistry.



RN 56-87-1 HCAPLUS

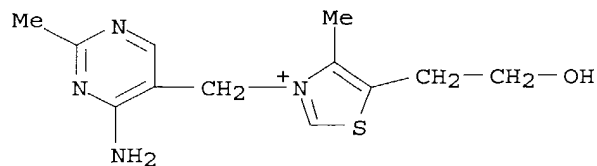
CN L-Lysine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 59-43-8 HCAPLUS

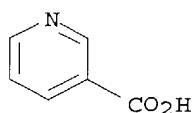
CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-4-methyl- chloride (9CI) (CA INDEX NAME)



● Cl⁻

RN 59-67-6 HCAPLUS

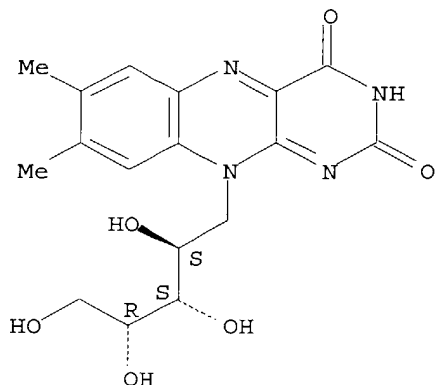
CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)



RN 83-88-5 HCAPLUS

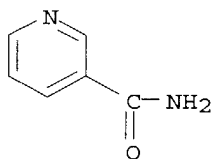
CN Riboflavin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 98-92-0 HCAPLUS

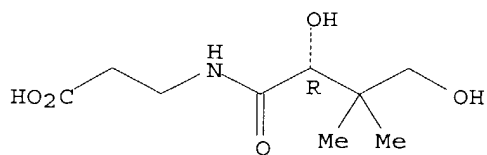
CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)



RN 137-08-6 HCAPLUS

CN β -Alanine, N-[(2R)-2,4-dihydroxy-3,3-dimethyl-1-oxobutyl]-, calcium salt (2:1) (9CI) (CA INDEX NAME)

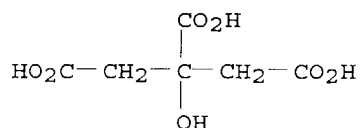
Absolute stereochemistry. Rotation (+).



● 1/2 Ca

RN 144-23-0 HCAPLUS

CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, magnesium salt (1:1) (9CI)
(CA INDEX NAME)

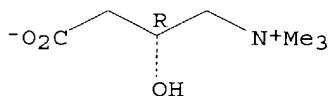


● Mg

RN 541-15-1 HCAPLUS

CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)-(9CI) (CA INDEX NAME)

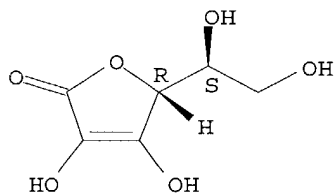
Absolute stereochemistry. Rotation (-).



RN 5743-27-1 HCAPLUS

CN L-Ascorbic acid, calcium salt (2:1) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 1/2 Ca

RN 7439-95-4 HCAPLUS

CN Magnesium (8CI, 9CI) (CA INDEX NAME)

Mg

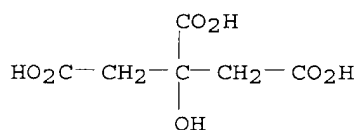
RN 7439-98-7 HCAPLUS

CN Molybdenum (8CI, 9CI) (CA INDEX NAME)

Mo

RN 7693-13-2 HCAPLUS

CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, calcium salt (9CI) (CA INDEX NAME)

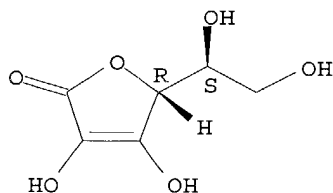


●x Ca

RN 15431-40-0 HCAPLUS

CN L-Ascorbic acid, magnesium salt (2:1) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



●1/2 Mg

L145 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:637513 HCAPLUS

DN 137:190730

ED Entered STN: 23 Aug 2002

TI **Compositions** of therapeutic biochemical compounds involved in **bioenergy** metabolism of cellsPA **Rath, Matthias, Neth.**

SO PCT Int. Appl., 16 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-194

ICS A61K031-122; A61K038-41; A61K031-198

CC 63-6 (**Pharmaceuticals**)

Section cross-reference(s): 1, 66

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002064129	A2	20020822	WO 2002-EP1545	20020214 <--
	WO 2002064129	A3	20030508		
	W: AE, AU, BR, CA, CN, CU, CZ, EE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	US 2002173546	A1	20021121	US 2002-77283	20020214 <--
	BR 2002003902	A	20030128	BR 2002-3902	20020214 <--
	EP 1368017	A2	20031210	EP 2002-719835	20020214 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
	NO 2002004536	A	20020920	NO 2002-4536	20020920 <--
PRAI	US 2001-268825P	P	20010214		<--

WO 2002-EP1545 W 20020214

- AB A **composition** of biochem. compds. involved in **bioenergy** metabolism of cells and a method of use in prevention and therapy of diseases are disclosed. The **composition** may contain 2 or more of the following biochem. substances, e.g., **succinate, fumarate, L-malate, α -ketoglutarate**, irresp. of their amts. for the improvement of cellular energy metabolism. These compds. may be administered at 0.001-100,000 mg.
- ST **bioenergy** metab cell biochem therapeutic
- IT **Energy metabolism, animal**
Human
 Tricarboxylic acid cycle
 Urea cycle
 (compns. of therapeutic biochem. compds. involved in **bioenergy** metabolism of cells)
- IT Drug delivery systems
 (infusions; compns. of therapeutic biochem. compds. involved in **bioenergy** metabolism of cells)
- IT Drug delivery systems
 (inhalants; compns. of therapeutic biochem. compds. involved in **bioenergy** metabolism of cells)
- IT Drug delivery systems
 (injections; compns. of therapeutic biochem. compds. involved in **bioenergy** metabolism of cells)
- IT Ubiquinones
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (reduced; compns. of therapeutic biochem. compds. involved in **bioenergy** metabolism of cells)
- IT Drug delivery systems
 (suppositories; compns. of therapeutic biochem. compds. involved in **bioenergy** metabolism of cells)
- IT Drug delivery systems
 (tablets; compns. of therapeutic biochem. compds. involved in **bioenergy** metabolism of cells)
- IT 50-81-7, **Ascorbic acid**, biological studies
53-57-6 53-59-8, **Nicotinamide-Adenine Dinucleotide Phosphate** 53-84-9,
Nicotinamide-Adenine Dinucleotide
56-65-5, **Adenosine Triphosphate**, biological studies 56-84-8, **L-Aspartic acid**, biological studies 56-87-1,
Lysine, biological studies 58-64-0, **Adenosine Diphosphate**, biological studies 58-68-4, **Reduced Nicotinamide Adenine Dinucleotide**
59-43-8, **Thiamine**, biological studies 59-67-6,
Nicotinic Acid, biological studies 70-26-8, **Ornithine** 72-89-9, **Acetyl-Coenzyme A** 74-79-3, **Arginine**, biological studies 77-92-9, **Citric acid**, biological studies 79-83-4, **Pantothenic acid** 83-88-5, **Riboflavin**, biological studies 86-01-1, **Guanosine Triphosphate** 89-00-9, **2,3-Pyridinedicarboxylic acid** 97-67-6, **L-Malic acid** 98-92-0,
Niacinamide 110-15-6, **Succinic acid**, biological studies 110-17-8, **Fumaric acid**, biological studies 127-17-3, **Pyruvic acid**, biological studies 146-14-5, **Flavin-Adenine Dinucleotide** 146-17-8, **Flavin Mononucleotide** 146-91-8, **Guanosine Diphosphate** 303-98-0, **Coenzyme Q-10** 320-77-4, **Isocitric acid** 328-42-7, **Oxalacetic acid** 328-50-7, **α -Ketoglutaric acid** 372-75-8, **Citrulline** 541-15-1, **Carnitine** 585-84-2, **cis-Aconitic acid** 604-98-8,

Succinyl-Coenzyme A 940-69-2,
 Lipoamide 1077-28-7, 1,2-Dithiolane-3-pentanoic acid
 1948-82-9, Oxalosuccinic acid 2387-71-5
 5666-16-0, Reduced Flavin
 Mononucleotide 7439-95-4, Magnesium, biological studies
 7439-96-5, Manganese, biological studies 7439-98-7,
 Molybdenum, biological studies 7440-50-8, Copper, biological
 studies 7440-70-2, Calcium, biological studies
 10124-49-9, Iron-Sulfate 14875-96-8, Heme b 26598-29-8, Heme c
 57560-10-8, Heme a 59890-88-9

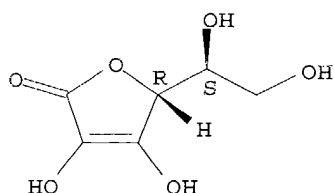
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compns. of therapeutic biochem. compds. involved in
 bioenergy metabolism of cells)

IT 50-81-7, Ascorbic acid, biological studies
 53-57-6 53-59-8, Nicotinamide-Adenine
 Dinucleotide Phosphate 53-84-9,
 Nicotinamide-Adenine Dinucleotide
 56-65-5, Adenosine Triphosphate, biological
 studies 56-87-1, Lysine, biological studies
 58-64-0, Adenosine Diphosphate, biological
 studies 58-68-4, Reduced Nicotinamide
 Adenine Dinucleotide 59-43-8, Thiamine
 , biological studies 59-67-6, Nicotinic Acid
 , biological studies 72-89-9, Acetyl-Coenzyme
 A 77-92-9, Citric acid, biological
 studies 79-83-4, Pantothenic acid
 83-88-5, Riboflavin, biological studies 86-01-1
 , Guanosine Triphosphate 89-00-9,
 2,3-Pyridinedicarboxylic acid 97-67-6, L-Malic
 acid 98-92-0, Niacinamide 110-15-6,
 Succinic acid, biological studies 110-17-8,
 Fumaric acid, biological studies 127-17-3,
 Pyruvic acid, biological studies 146-14-5,
 Flavin-Adenine Dinucleotide 146-17-8
 , Flavin Mononucleotide 146-91-8, Guanosine
 Diphosphate 320-77-4, Isocitric acid
 328-42-7, Oxalacetic acid 328-50-7,
 α -Ketoglutaric acid 541-15-1,
 Carnitine 585-84-2, cis-Aconitic
 acid 604-98-8, Succinyl-Coenzyme
 A 940-69-2, Lipoamide 1948-82-9,
 Oxalosuccinic acid 5666-16-0, Reduced
 Flavin Mononucleotide 7439-95-4, Magnesium,
 biological studies 7439-96-5, Manganese, biological studies
 7439-98-7, Molybdenum, biological studies
 7440-70-2, Calcium, biological studies 10124-49-9,
 Iron-Sulfate
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (compns. of therapeutic biochem. compds. involved in
 bioenergy metabolism of cells)

RN 50-81-7 HCAPLUS

CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

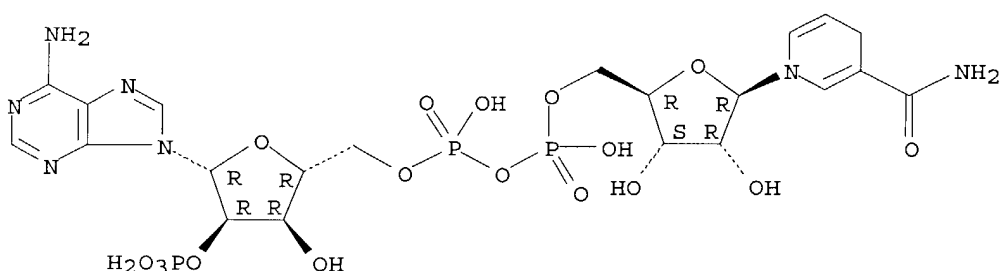
Absolute stereochemistry.



RN 53-57-6 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 2'-(dihydrogen phosphate),
P'→5'-ester with 1,4-dihydro-1-β-D-ribofuranosyl-3-
pyridinecarboxamide (9CI) (CA INDEX NAME)

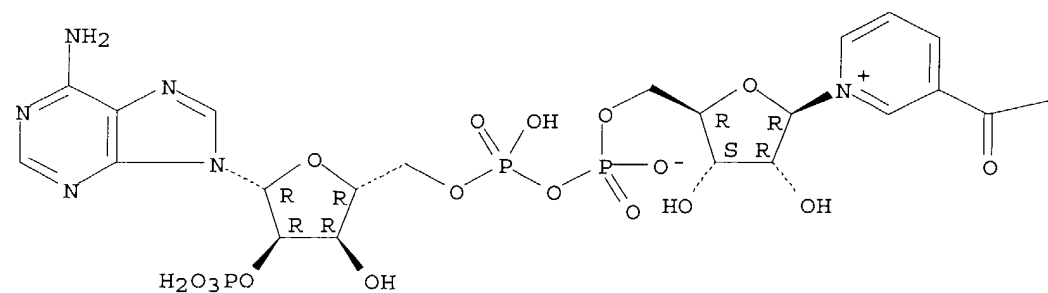
Absolute stereochemistry.



RN 53-59-8 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), 2'-(dihydrogen phosphate),
P'→5'-ester with 3-(aminocarbonyl)-1-β-D-
ribofuranosylpyridinium, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

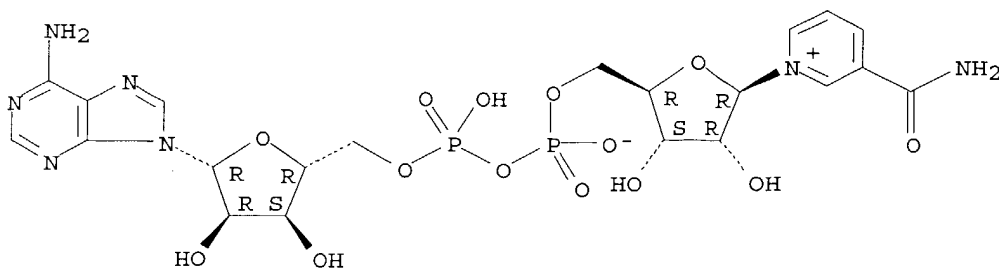
PAGE 1-B

—NH₂

RN 53-84-9 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), P'→5'-ester with
3-(aminocarbonyl)-1-β-D-ribofuranosylpyridinium, inner salt (9CI)
(CA INDEX NAME)

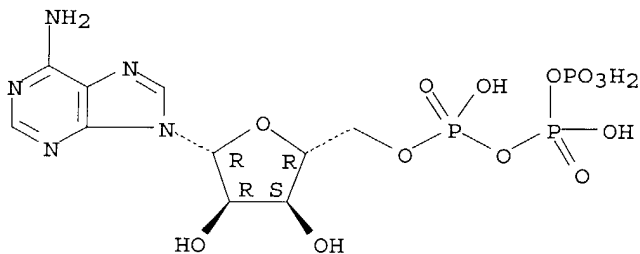
Absolute stereochemistry.



RN 56-65-5 HCAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

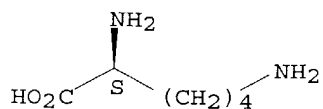
Absolute stereochemistry.



RN 56-87-1 HCAPLUS

CN L-Lysine (9CI) (CA INDEX NAME)

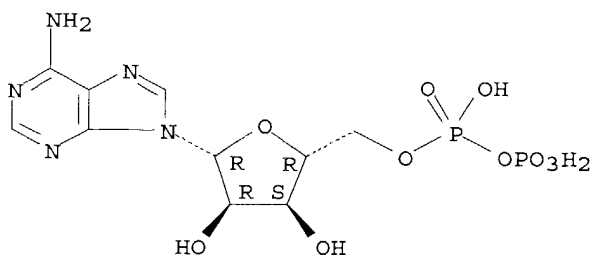
Absolute stereochemistry.



RN 58-64-0 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

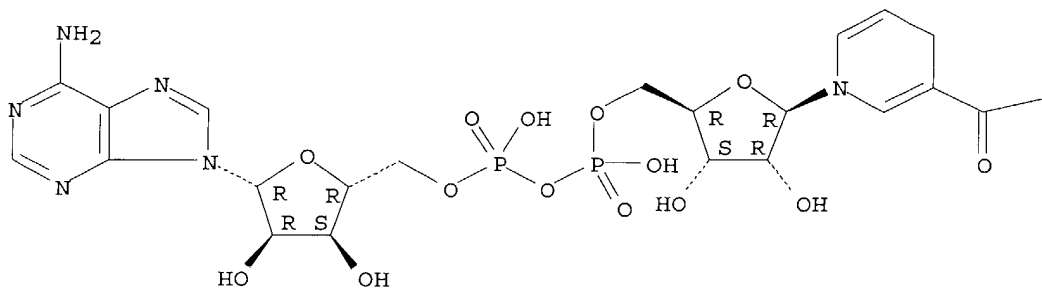
Absolute stereochemistry.



RN 58-68-4 HCAPLUS
 CN Adenosine 5'-(trihydrogen diphosphate), P'→5'-ester with
 1,4-dihydro-1-β-D-ribofuranosyl-3-pyridinecarboxamide (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.

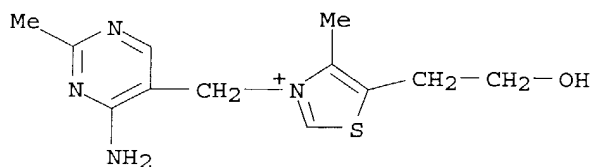
PAGE 1-A



PAGE 1-B

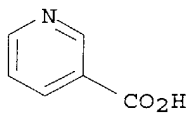
—NH₂

RN 59-43-8 HCAPLUS
 CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-
 4-methyl- chloride (9CI) (CA INDEX NAME)



● Cl⁻

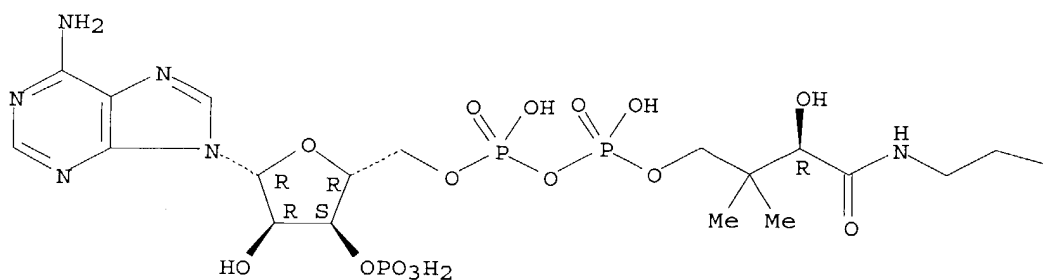
RN 59-67-6 HCAPLUS
 CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)



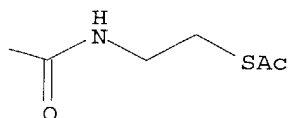
RN 72-89-9 HCAPLUS
 CN Coenzyme A, S-acetate (6CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

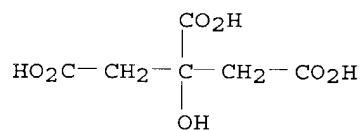
PAGE 1-A



PAGE 1-B

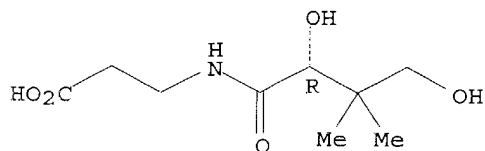


RN 77-92-9 HCAPLUS
CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy- (9CI) (CA INDEX NAME)



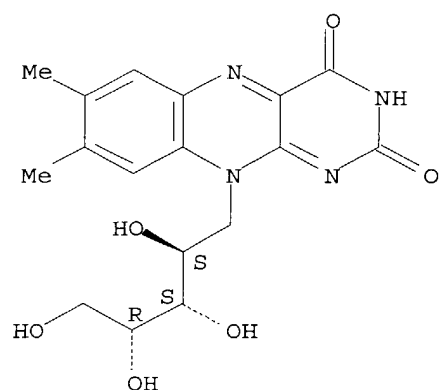
RN 79-83-4 HCAPLUS
CN β-Alanine, N-[(2R)-2,4-dihydroxy-3,3-dimethyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 83-88-5 HCAPLUS
CN Riboflavin (8CI, 9CI) (CA INDEX NAME)

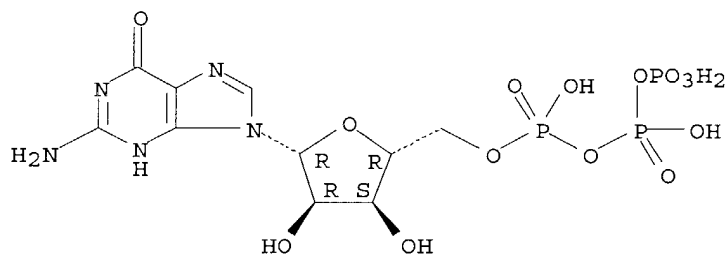
Absolute stereochemistry.



RN 86-01-1 HCAPLUS

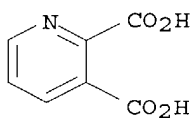
CN Guanosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 89-00-9 HCAPLUS

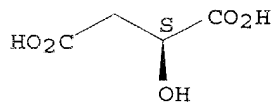
CN 2,3-Pyridinedicarboxylic acid (8CI, 9CI) (CA INDEX NAME)



RN 97-67-6 HCAPLUS

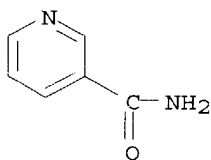
CN Butanedioic acid, hydroxy-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

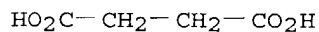


RN 98-92-0 HCAPLUS

CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)

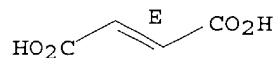


RN 110-15-6 HCAPLUS
CN Butanedioic acid (9CI) (CA INDEX NAME)

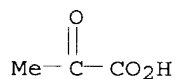


RN 110-17-8 HCAPLUS
CN 2-Butenedioic acid (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

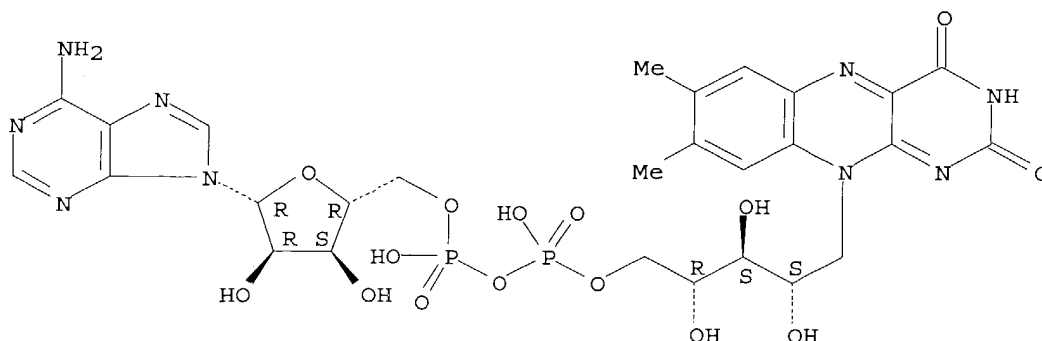


RN 127-17-3 HCAPLUS
CN Propanoic acid, 2-oxo- (9CI) (CA INDEX NAME)



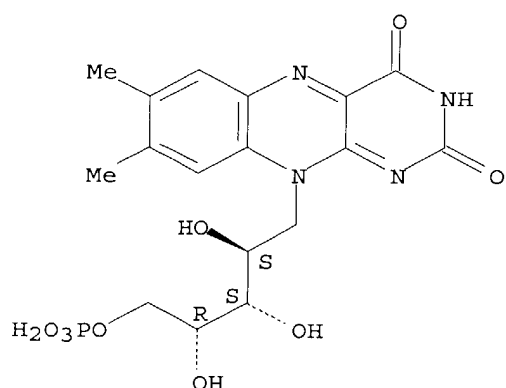
RN 146-14-5 HCAPLUS
CN Riboflavin 5'-(trihydrogen diphosphate), P'→5'-ester with adenosine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



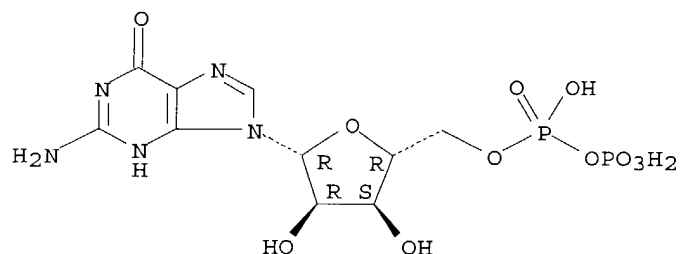
RN 146-17-8 HCAPLUS
CN Riboflavin 5'-(dihydrogen phosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

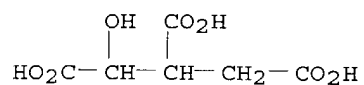


RN 146-91-8 HCAPLUS
 CN Guanosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

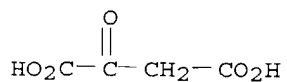
Absolute stereochemistry.



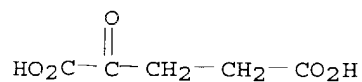
RN 320-77-4 HCAPLUS
 CN Pentaric acid, 3-carboxy-2,3-dideoxy- (9CI) (CA INDEX NAME)



RN 328-42-7 HCAPLUS
 CN Butanedioic acid, oxo- (9CI) (CA INDEX NAME)



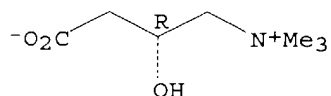
RN 328-50-7 HCAPLUS
 CN Pentanedioic acid, 2-oxo- (9CI) (CA INDEX NAME)



RN 541-15-1 HCAPLUS

CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)-
(9CI) (CA INDEX NAME)

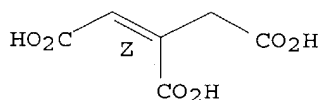
Absolute stereochemistry. Rotation (-).



RN 585-84-2 HCAPLUS

CN 1-Propene-1,2,3-tricarboxylic acid, (1Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

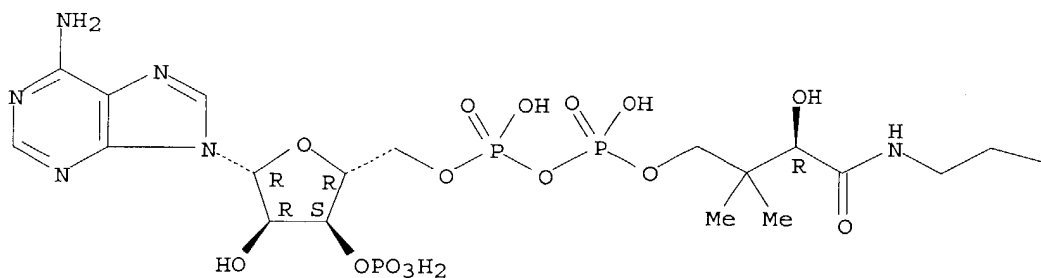


RN 604-98-8 HCAPLUS

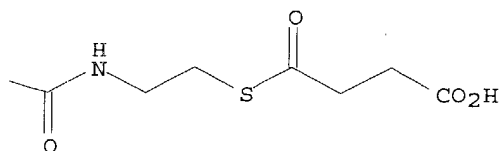
CN Coenzyme A, S-(hydrogen butanedioate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

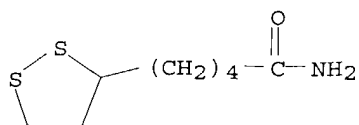


PAGE 1-B



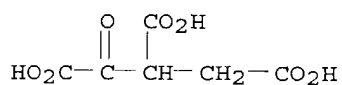
RN 940-69-2 HCAPLUS

CN 1,2-Dithiolane-3-pentanamide (9CI) (CA INDEX NAME)



RN 1948-82-9 HCAPLUS

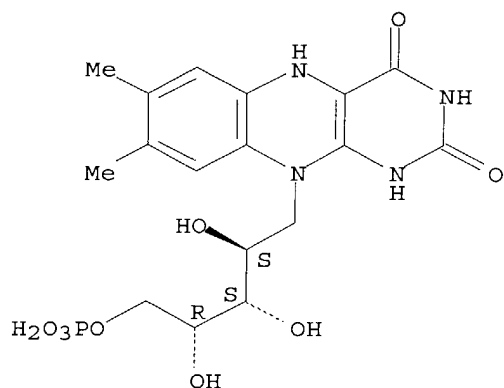
CN 1,2,3-Propanetricarboxylic acid, 1-oxo- (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 5666-16-0 HCAPLUS

CN Riboflavin 5'-(dihydrogen phosphate), 1,5-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 7439-95-4 HCAPLUS

CN Magnesium (8CI, 9CI) (CA INDEX NAME)

Mg

RN 7439-96-5 HCAPLUS

CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

RN 7439-98-7 HCAPLUS

CN Molybdenum (8CI, 9CI) (CA INDEX NAME)

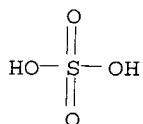
Mo

RN 7440-70-2 HCAPLUS

CN Calcium (8CI, 9CI) (CA INDEX NAME)

Ca

RN 10124-49-9 HCAPLUS
 CN Sulfuric acid, iron salt (8CI, 9CI) (CA INDEX NAME)



●x Fe(x)

L145 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:552171 HCAPLUS
 DN 137:99036
 ED Entered STN: 25 Jul 2002
 TI Synergistic compositions containing **ascorbate** and **lysine**
 for the treatment of extracellular matrix degeneration
 PA **Rath, Matthias, Neth.**
 SO Ger. Offen., 10 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 IC ICM A61K031-375
 ICS A61K031-198
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10101522	A1	20020725	DE 2001-10101522	20010115
PRAI	DE 2001-10101522		20010115		

AB The invention concerns synergistic pharmaceutical compns. that contain **ascorbate** and fibrinolysis/collagenase inhibitors from the group of **lysine** and its analogs for the prevention and treatment of extracellular matrix degeneration. The compns. further contain antioxidants. Thus typical oral compns. contain (mg/kgBw/d) and (IU/kgBw/d) resp.: **ascorbate** 5-500; EACA 1-1500; tranexamic acid 1-500; p-aminomethyl benzoic acid 1-500; **lysine** 1-1500; proline 1-1500; n-acetyl cysteine 0.1-5000; carotene 0.1-10 000; tocopherol 0.1-500.

ST synergism drug **ascorbate lysine** extracellular matrix degeneration

IT Extracellular matrix
 (degeneration; synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT Drug delivery systems
 (oral; synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT Drug delivery systems
 (parenterals; synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT Fibrinolysis
 (prevention of; synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT Cooperative phenomena
(synergism; synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT Atherosclerosis
Neoplasm
(synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT Tocopherols
Trace elements, biological studies
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT 9001-12-1, Collagenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

IT 50-81-7, **Ascorbic acid**, biological studies
56-87-1, L-**Lysine**, biological studies 56-91-7,
p-Aminomethyl benzoic acid 60-32-2, EACA 147-85-3, L-Proline,
biological studies 616-91-1, L-Cysteine, N-acetyl- 701-54-2,
Cyclohexanecarboxylic acid, 4-(aminomethyl)- 1197-18-8, Tranexamic acid
2393-24-0, p-Benzylamine sulfonic acid 6072-02-2, L-**Lysine**,
N2-acetyl-, methyl ester 7782-49-2, Selenium, biological studies
23288-49-5, Probutol 24306-54-5, 4-Aminomethyl-bicyclo-2,2,2-octane-1-
carboxylic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

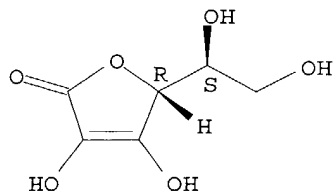
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Anon; DE 4243363 A1 HCAPLUS
(2) Anon; JP 4243825 A
(3) Anon; US 5639787 A HCAPLUS
(4) Anon; JP 62048622 A HCAPLUS
(5) Anon; JP 6256184 A
(6) Anon; JARC Sci Publ 1982, V41, P665

IT 50-81-7, **Ascorbic acid**, biological studies
56-87-1, L-**Lysine**, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic compns. containing **ascorbate** and **lysine** for treatment of extracellular matrix degeneration)

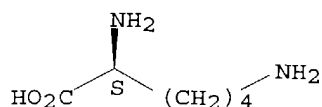
RN 50-81-7 HCAPLUS
CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 56-87-1 HCAPLUS
CN L-Lysine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L145 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:272794 HCAPLUS

DN 136:299725

ED Entered STN: 12 Apr 2002

TI Therapeutic **combination** of **ascorbate** with **lysine** or arginine for prevention and treatment of cancer

IN **Rath, Matthias**

PA Neth.

SO Eur. Pat. Appl., 12 pp.

CODEN: EPXXDW

DT **Patent**

LA English

IC ICM A61K031-195

ICS A61K031-375; A61P035-00

ICI A61K031-195, A61K031-375

CC 63-6 (**Pharmaceuticals**)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1195159	A1	20020410	EP 2000-121950	20001009 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	EP 2000-121950		20001009	<--	
AB	A therapeutic composition for the prevention and treatment of different forms of cancer in very elevated dosages of ascorbic acid and salts, L- Lysine and L-proline, vitamins and trace elements.				
ST	therapeutic combination ascorbate lysine antitumor; arginine ascorbate antitumor therapeutic combination				
IT	Flavonoids RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (biflavonoids; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)				
IT	Uterus, neoplasm (cervix, inhibitors; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)				
IT	Antitumor agents (cervix; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)				
IT	Intestine, neoplasm (duodenum, inhibitors; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)				
IT	Antitumor agents (duodenum; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)				
IT	Antitumor agents (esophagus; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)				

- cancer)
- IT Drug delivery systems
 - (inhalants; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Lung, neoplasm
- Ovary, neoplasm
- Skin, neoplasm
- Stomach, neoplasm
- Testis, neoplasm
 - (inhibitors; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Drug delivery systems
 - (injections; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (lung; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (mammary gland; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (melanoma; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Esophagus
- Mammary gland
 - (neoplasm, inhibitors; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (ovary; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (skin; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (small intestine; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Intestine, neoplasm
 - (small, inhibitors; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (stomach; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Drug delivery systems
 - (suppositories; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Drug delivery systems
 - (tablets; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Antitumor agents
 - (testis; therapeutic combination of ascorbate with lysine or arginine for prevention and treatment of cancer)
- IT Carotenes, biological studies
- Trace elements, biological studies
- Vitamins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combination of **ascorbate** with **lysine** or arginine for prevention and treatment of cancer)

IT 50-81-7, **Ascorbic acid**, biological studies
 56-40-6D, Glycine, chromium and **molybdenum** complexes
 56-87-1, L-**Lysine**, biological studies 58-56-0,
 Pyridoxine hydrochloride 58-85-5, Biotin 59-02-9, D- α -
 Tocopherol 59-30-3, Folic acid, biological studies 59-67-6,
 Niacin, biological studies 67-03-8, **Thiamine** hydrochloride
 67-97-0, Cholecalciferol 68-19-9, Cyanocobalamin 83-88-5,
Riboflavin, biological studies 87-89-8, Inositol 98-92-0
 , **Niacinamide** 119-13-1, δ -Tocopherol 127-40-2, Lutein
 137-08-6 137-66-6, **Ascorbyl** Palmitate 147-85-3,
 L-Proline, biological studies 148-03-8, β -Tocopherol 303-98-0,
 Coenzyme Q10 432-70-2, α -Carotene 472-70-8, Kryptoxanthin
 541-15-1, L-**Carnitine** 657-27-2, L-
Lysine hydrochloride 1119-34-2, L-Arginine hydrochloride
 3211-76-5, L-Selenomethionine 5743-27-1, Calcium
Ascorbate 7048-04-6, L-Cysteine hydrochloride monohydrate
 7235-40-7, β -Carotene 7439-96-5D, Manganese, chelates
 7439-98-7D, **Molybdenum**, glycinate complexes 7440-09-7,
 Potassium, biological studies 7440-47-3D, Chromium, glycinate complexes
 7616-22-0, γ -Tocopherol 7693-13-2, Calcium **citrate**
 7757-93-9, Dicalcium Phosphate 7779-25-1, Magnesium
citrate 13479-54-4, Copper glycinate 14281-83-5, Zinc
 glycinate 14451-00-4, Iron **fumarate** 14783-68-7
 15431-40-0, Magnesium **Ascorbate** 35947-07-0, Calcium
 glycinate 174882-69-0, Pycnogenol

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combination of **ascorbate** with **lysine** or arginine for prevention and treatment of cancer)

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE

- (1) Bio Nutritional Health Service; GB 2268871 A 1994 HCAPLUS
- (2) Bostom, A; PHARMACOTHERAPY 1995, V15(4), P458 MEDLINE
- (3) Dioguardi, F; US 5198465 A 1993 HCAPLUS
- (4) Dzau, V; US 5891459 A 1999 HCAPLUS
- (5) Health Now Inc; EP 0891771 A 1999 HCAPLUS
- (6) Katz, E; JOURNAL OF ORTHOMOLECULAR MEDICINE 1996, V11/3, P173
- (7) Novo Med Ag; DE 3440090 A 1986 HCAPLUS
- (8) Otsuka Pharma Co Ltd; GB 2029220 A 1980 HCAPLUS
- (9) Paul, S; US 5626883 A 1997 HCAPLUS
- (10) Rath, M; US 5278189 A 1994 HCAPLUS
- (11) Rath, M; US 5650418 A 1997 HCAPLUS

IT 50-81-7, **Ascorbic acid**, biological studies
 56-87-1, L-**Lysine**, biological studies 59-67-6,
 Niacin, biological studies 83-88-5, **Riboflavin**,
 biological studies 98-92-0, **Niacinamide**
 137-08-6 541-15-1, L-**Carnitine**
 657-27-2, L-**Lysine** hydrochloride 5743-27-1,
 Calcium **Ascorbate** 7439-96-5D, Manganese, chelates
 7439-98-7D, **Molybdenum**, glycinate complexes
 7693-13-2, Calcium **citrate** 7779-25-1,
 Magnesium **citrate** 14451-00-4, Iron **fumarate**
 15431-40-0, Magnesium **Ascorbate**

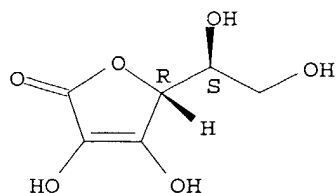
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combination of **ascorbate** with **lysine** or arginine for prevention and treatment of cancer)

RN 50-81-7 HCAPLUS

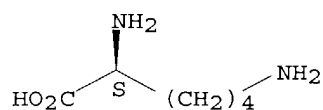
CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

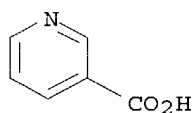


RN 56-87-1 HCAPLUS
CN L-Lysine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

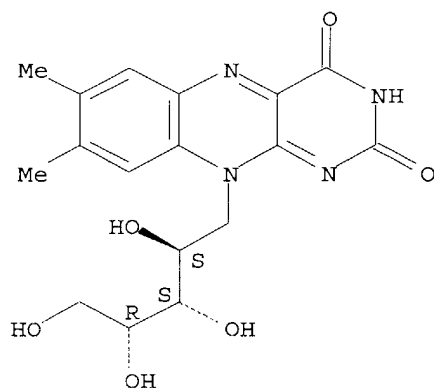


RN 59-67-6 HCAPLUS
CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)

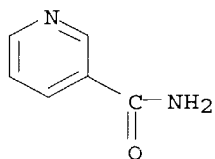


RN 83-88-5 HCAPLUS
CN Riboflavin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



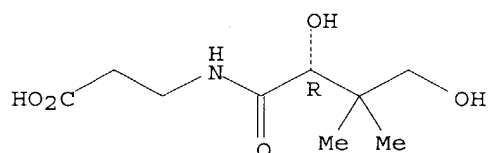
RN 98-92-0 HCAPLUS
CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)



RN 137-08-6 HCAPLUS

CN β -Alanine, N-[(2R)-2,4-dihydroxy-3,3-dimethyl-1-oxobutyl]-, calcium salt (2:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

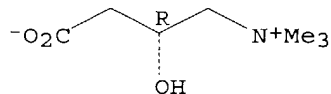


● 1/2 Ca

RN 541-15-1 HCAPLUS

CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)- (9CI) (CA INDEX NAME)

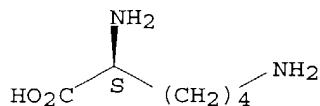
Absolute stereochemistry. Rotation (-).



RN 657-27-2 HCAPLUS

CN L-Lysine, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

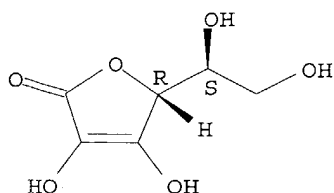


● HCl

RN 5743-27-1 HCAPLUS

CN L-Ascorbic acid, calcium salt (2:1) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 1/2 Ca

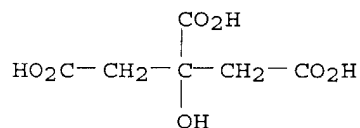
RN 7439-96-5 HCAPLUS
CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

RN 7439-98-7 HCAPLUS
CN Molybdenum (8CI, 9CI) (CA INDEX NAME)

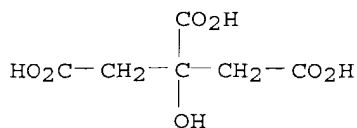
Mo

RN 7693-13-2 HCAPLUS
CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, calcium salt (9CI) (CA INDEX NAME)



● x Ca

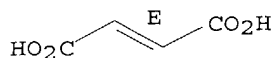
RN 7779-25-1 HCAPLUS
CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, magnesium salt (9CI) (CA INDEX NAME)



● x Mg

RN 14451-00-4 HCAPLUS
CN 2-Butenedioic acid (2E)-, iron salt (9CI) (CA INDEX NAME)

Double bond geometry as shown.

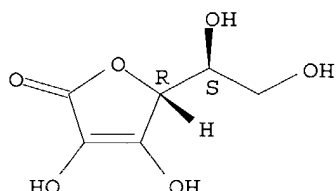


●x Fe(x)

RN 15431-40-0 HCAPLUS

CN L-Ascorbic acid, magnesium salt (2:1) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



●1/2 Mg

L145 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:918845 HCAPLUS

DN 136:42851

ED Entered STN: 21 Dec 2001

TI **Composition** for the prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium

IN **Rath, Matthias**

PA Neth.

SO Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DT **Patent**

LA English

IC ICM A61K031-195

ICS A61K031-375; A61K033-14; A61P009-00; A61P011-00; A61P027-00

ICI A61K031-195, A61K031-375

CC 63-6 (**Pharmaceuticals**)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1163904	A1	20011219	EP 2000-112811	20000616 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 2001003256	A	20020312	BR 2001-3256	20010613 <--
	NO 2001003004	A	20011217	NO 2001-3004	20010615 <--
	ZA 2001004931	A	20011220	ZA 2001-4931	20010615 <--
	CN 1333020	A	20020130	CN 2001-124330	20010615 <--
	JP 2002047183	A2	20020212	JP 2001-181658	20010615 <--
	NZ 512402	A	20030228	NZ 2001-512402	20010615 <--
PRAI	EP 2000-112811	A	20000616 <--		
AB	The invention relates to the use of biochem. substances for a composition for the prevention and treatment of health conditions				

caused by constriction of smooth muscle cells in organs of the human body like high blood pressure, asthma, glaucoma and tinnitus.

- ST smooth muscle disease **compn**; **ascorbate** smooth muscle disease **compn**; arginine smooth muscle disease **compn**; magnesium compd smooth muscle disease **compn**
- IT Flavonoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioflavonoids; **composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT Amino acids, biological studies
Carotenes, biological studies
Trace elements, biological studies
Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT Drug delivery systems
(infusions; **composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT Drug delivery systems
(inhalants; **composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT Drug delivery systems
(injections; **composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT Muscle, disease
(smooth; **composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT Drug delivery systems
(suppositories; **composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT Drug delivery systems
(tablets; **composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- IT 50-81-7, **Ascorbic acid**, biological studies
52-90-4, L-Cysteine, biological studies 56-40-6D, Glycine, complex with transition metals 56-87-1, L-Lysine, biological studies 58-85-5, Biotin 59-02-9, α -Tocopherol 59-30-3, Folic acid, biological studies 59-43-8, **Thiamine**, biological studies 59-67-6, Niacin, biological studies 65-23-6, Pyridoxine 67-97-0, Cholecalciferol 68-19-9, Cyanocobalamine 74-79-3, L-Arginine, biological studies 83-88-5, **Riboflavin**, biological studies 87-89-8, Inositol 98-92-0, **Niacinamide** 119-13-1, δ -Tocopherol 137-08-6, Calcium **pantothenate** 137-66-6, **Ascorbyl** palmitate 147-85-3, L-Proline, biological studies 148-03-8, β -Tocopherol 303-98-0, Coenzyme q10 541-15-1, L-Carnitine 3211-76-5, L-Selenomethionine 5743-27-1, Calcium **ascorbate** 7235-40-7, β -Carotene 7439-96-5D, Manganese, chelates 7439-98-7D, **Molybdenum**, complex with glycine 7440-09-7D, Potassium, chelates 7440-47-3D, Chromium, complex with glycine 7616-22-0, γ -Tocopherol 7693-13-2, Calcium **citrate** 7757-93-9, Dicalcium phosphate 7779-25-1, Magnesium **citrate** 13479-54-4, Copper glycinate 14281-83-5, Zinc glycinate 14783-68-7 15431-40-0, Magnesium **ascorbate** 35947-07-0, Calcium glycinate 174882-69-0, Pycnogenol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**composition** for prevention of smooth muscle diseases comprising **ascorbate**, arginine and magnesium)
- RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bio Nutritional Health Service; GB 2268871 A 1994 HCAPLUS

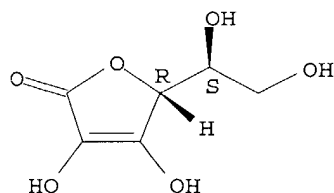
- (2) Bostom, A; Pharmacotherapy 1995, V15(4), P458 MEDLINE
- (3) Cooke, J; US 5891459 A 1999 HCAPLUS
- (4) Dioguardi Francesco, S; US 5198465 A 1993 HCAPLUS
- (5) Health Now Inc; EP 0891771 A 1999 HCAPLUS
- (6) Otsuka Pharma Co Ltd; GB 2029220 A 1980 HCAPLUS
- (7) Paul Stephen, M; US 5626883 A 1997 HCAPLUS
- (8) Rath, M; US 5650418 A 1997 HCAPLUS
- (9) Rath, M; Journal of Applied Nutrition 1996, V48/3(68-78)
- (10) Rath Matthias, W; US 5278189 A 1994 HCAPLUS

IT 50-81-7, **Ascorbic acid**, biological studies
 56-87-1, **L-Lysine**, biological studies 59-43-8,
Thiamine, biological studies 59-67-6, **Niacin**, biological
 studies 83-88-5, **Riboflavin**, biological studies
 98-92-0, **Niacinamide** 137-08-6, **Calcium**
pantothenate 541-15-1, **L-Carnitine**
 5743-27-1, **Calcium ascorbate** 7439-96-5D,
 Manganese, chelates 7439-98-7D, **Molybdenum**, complex
 with glycine 7693-13-2, **Calcium citrate**
 7779-25-1, **Magnesium citrate** 15431-40-0,
Magnesium ascorbate
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (composition for prevention of smooth muscle diseases comprising
ascorbate, arginine and magnesium)

RN 50-81-7 HCAPLUS

CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

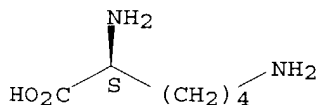
Absolute stereochemistry.



RN 56-87-1 HCAPLUS

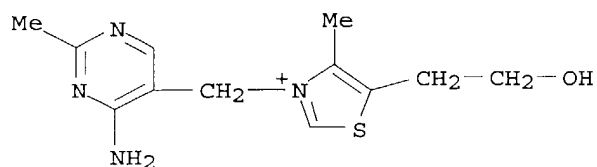
CN L-Lysine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

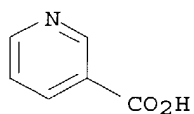


RN 59-43-8 HCAPLUS

CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-
 4-methyl- chloride (9CI) (CA INDEX NAME)

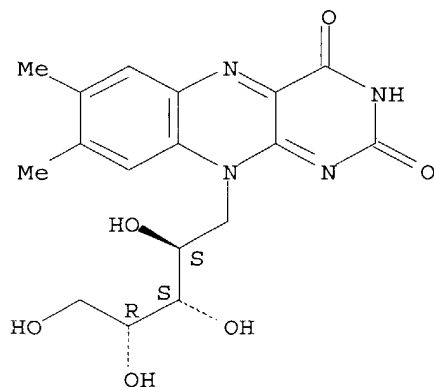


RN 59-67-6 HCAPLUS
 CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)

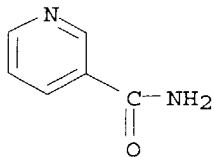


RN 83-88-5 HCAPLUS
 CN Riboflavin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

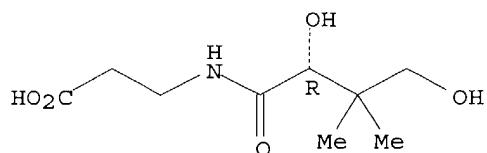


RN 98-92-0 HCAPLUS
 CN 3-Pyridinecarboxamide (9CI) (CA INDEX NAME)



RN 137-08-6 HCAPLUS
 CN β-Alanine, N-[(2R)-2,4-dihydroxy-3,3-dimethyl-1-oxobutyl]-, calcium salt (2:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

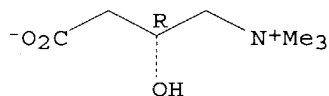


● 1/2 Ca

RN 541-15-1 HCAPLUS

CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)-
(9CI) (CA INDEX NAME)

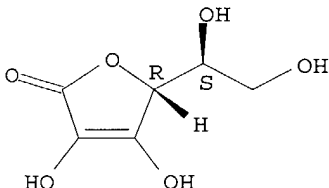
Absolute stereochemistry. Rotation (-).



RN 5743-27-1 HCAPLUS

CN L-Ascorbic acid, calcium salt (2:1) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



● 1/2 Ca

RN 7439-96-5 HCAPLUS

CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

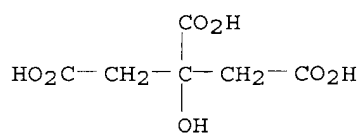
RN 7439-98-7 HCAPLUS

CN Molybdenum (8CI, 9CI) (CA INDEX NAME)

Mo

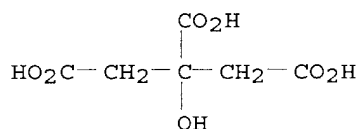
RN 7693-13-2 HCAPLUS

CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, calcium salt (9CI) (CA INDEX NAME)



●x Ca

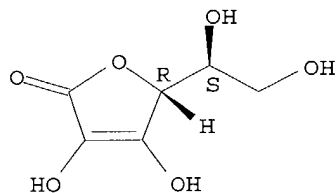
RN 7779-25-1 HCAPLUS
 CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, magnesium salt (9CI) (CA INDEX NAME)



●x Mg

RN 15431-40-0 HCAPLUS
 CN L-Ascorbic acid, magnesium salt (2:1) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



●1/2 Mg

L145 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:429714 HCAPLUS

DN 131:266358

ED Entered STN: 13 Jul 1999

TI **Pyruvate** and **hydroxycitrate/carnitine** may synergize to promote reverse electron transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids

AU McCarty, M. F.; Gustin, J. C.

CS NutriGuard Research, Encinitas, CA, 92024, USA

SO Medical Hypotheses (1999), 52(5), 407-416

CODEN: MEHYDY; ISSN: 0306-9877

PB Churchill Livingstone

DT Journal; General Review

LA English

CC 1-0 (Pharmacology)

Section cross-reference(s): 18

- AB A review with 97 refs. containing an informal pilot trial with new data. In a recent pilot study, joint administration of **pyruvate**, **hydroxycitrate** (HCA), and **carnitine** to obese subjects was associated with a remarkable rate of body-fat loss and thermogenesis, strongly suggestive of uncoupled fatty-acid oxidation. Hepatocytes possess an uncoupling mechanism - reverse electron transport - that enables fasting ketogenesis to proceed independent of respiratory control. Electrons entering the respiratory chain at the coenzyme Q (CoQ) level via **FAD**-dependent acyl coA dehydrogenase, can be driven "up" the chain by the electrochem. proton gradient to reduce NAD⁺; if these electrons are then shuttled to the cytoplasm, returning to the respiratory chain at the CoQ level, the net result is heat generation at the expense of the proton gradient, enabling the uncoupled flow of electrons to oxygen. **Pyruvate's** bariatric utility may stem from its ability to catalyze the rapid transport of high-energy electrons from mitochondria to the cytoplasm, thus stimulating electron shuttle mechanisms. By enabling rapid mitochondrial uptake of fatty acids and thus disinhibiting hepatocyte ketogenesis, HCA/**carnitine** should initiate reverse electron transport: concurrent amplification of electron shuttle mechanisms by **pyruvate** can be expected to accelerate this reverse electron transport, thereby decreasing the electrochem. proton gradient. As a result, hepatocytes may be able to convert fatty acids to CO₂ and heat with little net generation of ATP. These considerations suggest that it may be feasible to render hepatocytes functionally equivalent to activated brown fat, such that stored fat can be selectively oxidized in the absence of caloric restriction. Other measures which enhance the efficiency of hepatocyte electron shuttle mechanisms may increase the efficacy of this strategy.
- ST review **pyruvate hydroxycitrate carnitine** lipolysis
- IT Lipids, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (lipolysis; **pyruvate** and **hydroxycitrate/carnitine** may **synergize** to promote reverse electron transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids)
- IT **Respiration, animal**
 (mitochondrial; **pyruvate** and **hydroxycitrate/carnitine** may **synergize** to promote reverse electron transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids)
- IT Fatty acids, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (oxidation; **pyruvate** and **hydroxycitrate/carnitine** may **synergize** to promote reverse electron transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids)
- IT Antiobesity agents
 (**pyruvate** and **hydroxycitrate/carnitine** may **synergize** to promote reverse electron transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids)
- IT Drug interactions
 (**synergistic**; **pyruvate** and **hydroxycitrate/carnitine** may **synergize** to promote reverse electron transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids)
- IT Diet
 (therapeutic; **pyruvate** and **hydroxycitrate/carnitine** may **synergize** to promote reverse electron

transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids)

IT 127-17-3, biological studies 541-15-1, Carnitine

27750-10-3, Hydroxycitric acid

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pyruvate and hydroxycitrate/carnitine

may synergize to promote reverse electron transport in hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty acids)

RE.CNT 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Agius, L; Eur J Biochem 1985, V152, P699 HCAPLUS
- (2) Anon; Nutr Rev 1970, V28, P242
- (3) Argaud, D; Eur J Biochem 1993, V213, P1341 HCAPLUS
- (4) Berry, M; Eur J Biochem 1983, V131, P205 HCAPLUS
- (5) Berry, M; Metabolism 1985, V34, P141 HCAPLUS
- (6) Bjorntorp, P; Arteriosclerosis 1990, V10, P493 MEDLINE
- (7) Bjorntorp, P; Diab Care 1991, V14, P1132 MEDLINE
- (8) Bjorvell, H; Int J Obesity 1984, V8, P129 MEDLINE
- (9) Bobyleva, V; Biochem Biophys Acta 1997, V341, P122 HCAPLUS
- (10) Bobyleva, V; J Bioenerg Biomemb 1993, V25, P313 HCAPLUS
- (11) Bobyleva-Guarriero, V; Arch Biochem Biophys 1986, V245, P477 HCAPLUS
- (12) Boden, G; Diabetes 1996, V45, P3
- (13) Borboni, P; Acta Diabetol 1996, V33, P154 HCAPLUS
- (14) Broomfield, P; N Engl J Med 1988, V319, P1567 MEDLINE
- (15) Buemann, B; Sports Med 1996, V21, P191 MEDLINE
- (16) Chance, B; Nature 1960, V185, P666 HCAPLUS
- (17) Chauhan, J; J Biol Chem 1991, V266, P10035 HCAPLUS
- (18) Cheifetz, P; Metabolism 1965, V14, P1267 HCAPLUS
- (19) Clarke, B; Br Med J 1977, V2, P1567
- (20) Clarke, B; Lancet 1968, Vi, P123
- (21) Conway, J; Am J Clin Nutr 1984, V40, P1123 MEDLINE
- (22) Cortez, M; Am J Clin Nutr 1991, V53, P847 HCAPLUS
- (23) Cusi, K; J Clin Endocrinol Metab 1996, V81, P4059 HCAPLUS
- (24) Dakshinamurti, K; Arch Biochem Biophys 1968, V127, P17 HCAPLUS
- (25) Debeer, L; Eur J Biochem 1974, V47, P591 HCAPLUS
- (26) Elia, M; Eur J Clin Nutr 1990, V44, P113 MEDLINE
- (27) Feliu, J; Proc Natl Acad Sci 1976, V73, P2762 HCAPLUS
- (28) Ferrannini, E; J Clin Invest 1983, V72, P1737 HCAPLUS
- (29) Folkers, K; J Med 1978, V9, P67 MEDLINE
- (30) Fujioka, S; Int J Obesity 1991, V15, P853 MEDLINE
- (31) Halestrap, A; Biochim Biophys Acta 1987, V927, P280 HCAPLUS
- (32) Hoy, M; Am J Clin Nutr 1994, V60, P249 MEDLINE
- (33) Hue, L; Adv Enzymol 1981, V52, P247 HCAPLUS
- (34) Jackson, R; Diabetes 1987, V36, P632 MEDLINE
- (35) Kaats, G; 3rd International Conference on Anti-Aging Medicine and Biomedical Technology 1995
- (36) Kaats, G; Curr Ther Res 1996, V57, P747 HCAPLUS
- (37) Kaats, G; Manuscript in submission 1997
- (38) Klingenberg, M; Biochem Z 1961, V335, P243 HCAPLUS
- (39) Lardy, H; Ann Rev Biochem 1990, V59, P689 HCAPLUS
- (40) Lardy, H; Proc Natl Acad Sci 1995, V92, P6617 HCAPLUS
- (41) Larsen, T; Acta Physiol Scand 1983, V117, P451 HCAPLUS
- (42) Lee, A; Diabetes 1996, V45(Suppl 2), P170A
- (43) Leibel, R; Metabolism 1980, V29, P1234 MEDLINE
- (44) Liddle, R; Arch Intern Med 1989, V149, P1750 MEDLINE
- (45) Ljungstrom, O; Eur J Biochem 1976, V68, P497 HCAPLUS
- (46) Lowenstein, N; J Biol Chem 1971, V246, P629
- (47) Mabrouk, G; J Biol Chem 1990, V265, P6330 HCAPLUS
- (48) Maebashi, M; J Clin Biochem Nutr 1993, V14, P211
- (49) Matschinsky, F; Diabetes 1996, V45, P223 HCAPLUS

- (50) McCarty, M; Med Hypotheses 1994, V42, P215 HCAPLUS
- (51) McCarty, M; Med Hypotheses 1995, V45, P247 HCAPLUS
- (52) McCarty, M; Med Hypotheses 1995, V44, P278 MEDLINE
- (53) McCarty, M; Med Hypotheses 1997, V52, P89
- (54) McCarty, M; Med Hypotheses 1998, V51, P399 HCAPLUS
- (55) McGarry, J; Ann Rev Biochem 1980, V49, P395 HCAPLUS
- (56) McGarry, J; J Biol Chem 1979, V254, P8163 HCAPLUS
- (57) McGarry, J; Proc Natl Acad Sci 1975, V72, P4385 HCAPLUS
- (58) Messing, B; Gastroenterology 1983, V84, P1012 MEDLINE
- (59) Nair, K; J Clin Endocrinol 1987, V64, P896 HCAPLUS
- (60) Packer, L; J Biol Chem 1962, V237, P1327 HCAPLUS
- (61) Paolisso, G; Diabetologia 1995, V38, P1213 HCAPLUS
- (62) Papa, S; Eur J Biochem 1974, V49, P265 HCAPLUS
- (63) Pegorier, J; Biochem J 1989, V264, P93 HCAPLUS
- (64) Rebrin, K; J Clin Invest 1996, V98, P741 HCAPLUS
- (65) Ross, R; Am J Clin Nutr 1994, V60, P695 MEDLINE
- (66) Runcie, J; Postgrad Med J 1969, V45, P251 MEDLINE
- (67) Scholes, T; Biochemistry 1984, V23, P3341 HCAPLUS
- (68) Scholz, R; Eur J Biochem 1984, V141, P223 HCAPLUS
- (69) Shepherd, M; Diabetes 1994, V43(Suppl 1), P74A
- (70) Snoswell, A; Biochim Biophys Acta 1962, V60, P143 HCAPLUS
- (71) Spence, J; J Biol Chem 1984, V259, P6363
- (72) Stanko, R; Am J Clin Nutr 1992, V56, P630 HCAPLUS
- (73) Stanko, R; Am J Clin Nutr 1992, V55, P771 MEDLINE
- (74) Stanko, R; Am J Clin Nutr 1994, V59, P423 MEDLINE
- (75) Stanko, R; Int J Obesity 1996, V20, P925 HCAPLUS
- (76) Stanko, R; J Animal Sci 1989, V67, P1272 HCAPLUS
- (77) Stanko, R; J Appl Physiol 1990, V68, P119 HCAPLUS
- (78) Stanko, R; J Appl Physiol 1990, V69, P1651 HCAPLUS
- (79) Stanko, R; J Lab Clin Med 1978, V91, P228 HCAPLUS
- (80) Stanko, R; Metabolism 1986, V35, P182 HCAPLUS
- (81) Stirling, J; Nature 1968, V220, P801 HCAPLUS
- (82) Stummvoll, M; N Engl J Med 1995, V333, P550 HCAPLUS
- (83) Sullivan, A; Biochemical Pharmacology of Obesity 1983, P311 HCAPLUS
- (84) Tyzbir, R; J Nutr 1981, V111, P252 HCAPLUS
- (85) Van Gaal, L; Biomedical and Clinical Aspects of Coenzyme Q 1984, V4, P369
- (86) Vaulont, S; FASEB J 1994, V8, P28 HCAPLUS
- (87) Vesely, D; Science 1982, V216, P1329 HCAPLUS
- (88) Watson, J; Arch Biochem Biophys 1969, V135, P209 HCAPLUS
- (89) Wattchow, D; Br Med J 1983, V286, P763 MEDLINE
- (90) Wernette, M; J Biol Chem 1981, V256, P12767 MEDLINE
- (91) Williamson, J; Adv Enzyme Reg 1968, V6, P67 HCAPLUS
- (92) Wirtshafter, D; Science 1977, V198, P1271 HCAPLUS
- (93) Yamazaki, R; J Biol Chem 1975, V250, P7924 HCAPLUS
- (94) Yang, H; Dig Dis Sci 1992, V37, P912 MEDLINE
- (95) Zamboni, M; Am J Clin Nutr 1993, V58, P29 MEDLINE
- (96) Zhang, H; 16th International Congress of Nutrition 1997, P264 HCAPLUS
- (97) Zhang, H; J Nutr Sci Vitaminol 1996, V42, P517 HCAPLUS

IT 127-17-3, biological studies 541-15-1, Carnitine

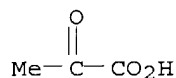
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(pyruvate and hydroxycitrate/carnitine

may synergize to promote reverse electron transport in
hepatocyte mitochondria, effectively "uncoupling" the oxidation of fatty
acids)

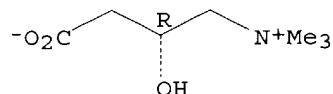
RN 127-17-3 HCAPLUS

CN Propanoic acid, 2-oxo- (9CI) (CA INDEX NAME)



RN 541-15-1 HCAPLUS
 CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L145 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:297312 HCAPLUS
 DN 130:320858
 ED Entered STN: 14 May 1999
 TI Nutritional supplement for cerebral metabolic insufficiencies
 IN Blass, John P.
 PA Cornell Research Foundation, Inc., USA
 SO PCT Int. Appl., 27 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K031-70
 ICS A61K031-715; A61K031-19
 CC 1-11 (Pharmacology)
 Section cross-reference(s): 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9921565	A1	19990506	WO 1998-US18120	19980901 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306875	AA	19990506	CA 1998-2306875	19980901 <--
AU 9892139	A1	19990517	AU 1998-92139	19980901 <--
AU 760140	B2	20030508		
EP 1032403	A1	20000906	EP 1998-944644	19980901 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001521002	T2	20011106	JP 2000-517723	19980901 <--
US 6537969	B1	20030325	US 2000-529091	20001020 <--
US 2003176365	A1	20030918	US 2003-379816	20030304 <--
PRAI US 1997-63165P	P	19971024	<--	
WO 1998-US18120	W	19980901	<--	
US 2000-529091	A1	20001020	<--	
AB	The present invention relates to a pharmaceutical composition which includes a sugar and a Krebs cycle intermediate, or salt thereof, or a precursor of a Krebs cycle intermediate. Krebs cycle intermediates include citric acid, aconitic acid, isocitric			

acid, α -ketoglutaric, succinic acid, fumaric acid, malic acid, and oxaloacetic acid, and mixts. thereof. Precursors of **Krebs cycle** intermediates are compds. converted by the body to form a **Krebs cycle** intermediate. The present invention also relates to administration of the pharmaceutical composition to treat an individual for a disorder involving impaired mitochondrial function and to improve cerebral function in an individual having impaired cerebral metabolism

- ST nutritional supplement saccharide **Krebs cycle** intermediate; cerebral metabolic insufficiency glucose malate
- IT Nervous system
(Huntington's chorea; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Glutamate antagonists
(NMDA antagonists; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Antioxidants
(as adjuvant; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Minerals, biological studies
Vitamins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as adjuvant; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Heart, disease
(cardiomyopathy; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Mental disorder
(depression, neurotic; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Mental disorder
(depression; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Cardiovascular system
(disease; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Heart, disease
(failure; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Mitochondria
(function enhancement in; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Drug delivery systems
(injections, i.m.; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Drug delivery systems
(injections, i.v.; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)

- IT Drug delivery systems
(injections, s.c.; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Brain, disease
(insufficiency; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Drug delivery systems
(mucosal; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Drug delivery systems
(nasal; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Alzheimer's disease
Atherosclerosis
Musculoskeletal diseases
Nutrients
Parkinson's disease
Tricarboxylic acid cycle
(nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Disaccharides
Monosaccharides
Polysaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Drug delivery systems
(oral; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Drug delivery systems
(parenterals; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Mental disorder
(psychosis; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Drug delivery systems
(solns., i.p.; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Nervous system
(spinocerebellar ataxia; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT Heart, disease
Heart, disease
(valve; nutritional supplements containing sugars and **Krebs cycle** intermediates for improving impaired mitochondrial functions)
- IT 77-92-9D, Citric acid, esters
110-15-6D, Succinic acid, esters
110-17-8D, Fumaric acid, esters
320-77-4D, Isocitric acid, esters

328-42-7D, Oxaloacetic acid, esters 328-50-7D,
 α -Ketoglutaric acid, esters 499-12-7D,
 Aconitic acid, esters 6915-15-7D, Malic acid, esters
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (Krebs cycle intermediate precursor; nutritional
 supplements containing sugars and Krebs cycle
 intermediates for improving impaired mitochondrial functions)

IT 57-00-1, Creatine 59-43-8, Thiamine, biological
 studies 59-67-6, Niacin, biological studies 65-23-6,
 Pyridoxine 79-83-4, Pantothenic acid
 83-88-5, Riboflavin, biological studies 541-15-1
 , L-Carnitine
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (as adjuvant; nutritional supplements containing sugars and Krebs
 cycle intermediates for improving impaired mitochondrial
 functions)

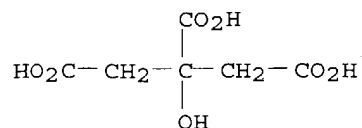
IT 9000-81-1, Acetylcholinesterase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; nutritional supplements containing sugars and Krebs
 cycle intermediates for improving impaired mitochondrial
 functions)

IT 50-99-7, Glucose, biological studies 56-84-8, L-Aspartic acid,
 biological studies 57-48-7, Fructose, biological studies 57-50-1,
 Sucrose, biological studies 59-23-4, Galactose, biological studies
 63-42-3, Lactose 69-79-4, Maltose 77-92-9, Citric
 acid, biological studies 110-15-6, Succinic
 acid, biological studies 110-17-8, Fumaric
 acid, biological studies 140-86-3 320-77-4,
 Isocitric acid 328-42-7, Oxaloacetic
 acid 328-50-7, α -Ketoglutaric
 acid 499-12-7, Aconitic acid 1518-62-3,
 2,4-Dihydroxybutyric acid 3068-00-6, 1,2,4-Butanetriol 3458-28-4,
 Mannose 6915-15-7, Malic acid 9005-25-8, Starch, biological
 studies 22136-38-5, 2-keto-4-Hydroxybutyric acid
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (nutritional supplements containing sugars and Krebs
 cycle intermediates for improving impaired mitochondrial
 functions)

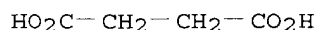
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE
 (1) Umezawa; US 3963579 A 1976 HCAPLUS
 (2) Yokota, K; Nippon Iyo Masu Supekutoru Gakkai Koenshu 1992, V17, P55 HCAPLUS

IT 77-92-9D, Citric acid, esters
 110-15-6D, Succinic acid, esters
 110-17-8D, Fumaric acid, esters
 320-77-4D, Isocitric acid, esters
 328-42-7D, Oxaloacetic acid, esters 328-50-7D,
 α -Ketoglutaric acid, esters
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (Krebs cycle intermediate precursor; nutritional
 supplements containing sugars and Krebs cycle
 intermediates for improving impaired mitochondrial functions)

RN 77-92-9 HCAPLUS
 CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy- (9CI) (CA INDEX NAME)

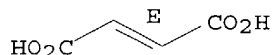


RN 110-15-6 HCAPLUS
CN Butanedioic acid (9CI) (CA INDEX NAME)

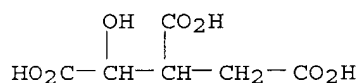


RN 110-17-8 HCAPLUS
CN 2-Butenedioic acid (2E)- (9CI) (CA INDEX NAME)

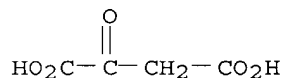
Double bond geometry as shown.



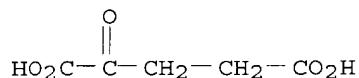
RN 320-77-4 HCAPLUS
CN Pentaric acid, 3-carboxy-2,3-dideoxy- (9CI) (CA INDEX NAME)



RN 328-42-7 HCAPLUS
CN Butanedioic acid, oxo- (9CI) (CA INDEX NAME)

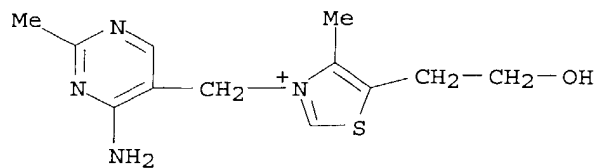


RN 328-50-7 HCAPLUS
CN Pentanedioic acid, 2-oxo- (9CI) (CA INDEX NAME)



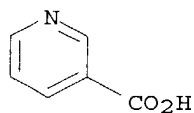
IT 59-43-8, **Thiamine**, biological studies 59-67-6,
Niacin, biological studies 79-83-4, **Pantothenic**
acid 83-88-5, **Riboflavin**, biological studies
541-15-1, **L-Carnitine**
RL: **BAC (Biological activity or effector, except adverse)**; BSU
(Biological study, unclassified); **THU (Therapeutic use)**; BIOL
(Biological study); **USES (Uses)**
(as adjuvant; nutritional supplements containing sugars and **Krebs**
cycle intermediates for improving impaired mitochondrial
functions)
RN 59-43-8 HCAPLUS
CN Thiazolium, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-5-(2-hydroxyethyl)-

4-methyl- chloride (9CI) (CA INDEX NAME)



RN 59-67-6 HCAPLUS

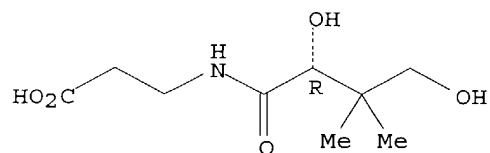
CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)



RN 79-83-4 HCAPLUS

CN β -Alanine, N-[(2R)-2,4-dihydroxy-3,3-dimethyl-1-oxobutyl]- (9CI) (CA INDEX NAME)

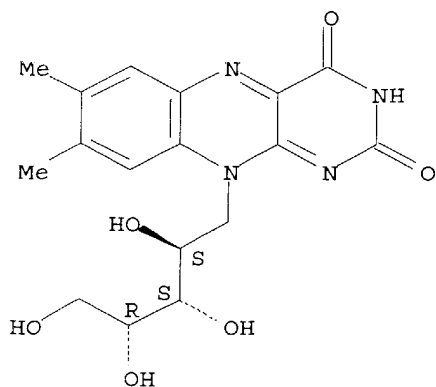
Absolute stereochemistry. Rotation (+).



RN 83-88-5 HCAPLUS

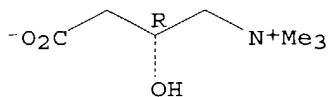
CN Riboflavin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



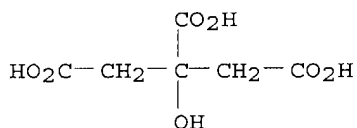
RN 541-15-1 HCAPLUS
 CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

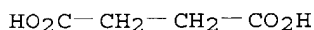


IT 77-92-9, Citric acid, biological studies
 110-15-6, Succinic acid, biological studies
 110-17-8, Fumaric acid, biological studies
 320-77-4, Isocitric acid 328-42-7,
 Oxaloacetic acid 328-50-7, α -
 Ketoglutaric acid
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (nutritional supplements containing sugars and Krebs
 cycle intermediates for improving impaired mitochondrial
 functions)

RN 77-92-9 HCAPLUS
 CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy- (9CI) (CA INDEX NAME)

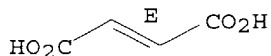


RN 110-15-6 HCAPLUS
 CN Butanedioic acid (9CI) (CA INDEX NAME)

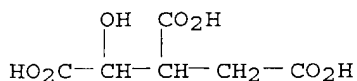


RN 110-17-8 HCAPLUS
 CN 2-Butenedioic acid (2E)- (9CI) (CA INDEX NAME)

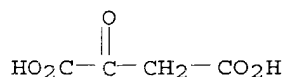
Double bond geometry as shown.



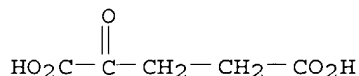
RN 320-77-4 HCAPLUS
 CN Pentaric acid, 3-carboxy-2,3-dideoxy- (9CI) (CA INDEX NAME)



RN 328-42-7 HCAPLUS
 CN Butanedioic acid, oxo- (9CI) (CA INDEX NAME)



RN 328-50-7 HCAPLUS
 CN Pentanedioic acid, 2-oxo- (9CI) (CA INDEX NAME)



L145 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN
 AN 1999:70355 HCAPLUS
 DN 130:129986
 ED Entered STN: 02 Feb 1999
 TI Compositions comprising **lysine** and **ascorbate** compounds
 for the treatment and prevention of cardiovascular diseases
 IN **Rath, Matthias**
 PA Health Now, Inc., USA
 SO Eur. Pat. Appl., 14 pp.
 CODEN: EPXXDW
 DT **Patent**
 LA English
 IC ICM A61K031-195
 ICS A61K031-375
 ICI A61K031-195, A61K031-375, A61K031-40, A61K031-59
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1, 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 891771	A1	19990120	EP 1997-304994	19970708
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EP 1068868	A2	20010117	EP 2000-115643	19970708
	EP 1068868	A3	20010131		
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
	NZ 509295	A	20021220	NZ 2001-509295	20010110
	HR 2001000023	A1	20020831	HR 2001-23	20010111
	HR 20010023	B1	20031231		
PRAI	EP 1997-304994	A	19970708		

AB A therapeutic **lysine**-based composition and methods for its use in the prevention and treatment of cardiovascular disease is disclosed. The composition includes at least one **lysine** compound such as **lysine**, **lysine** hydrochloride, **lysine** dihydrochloride, **lysine** orotate, **lysine** succinate, or **lysine** glutamate. The composition may also preferentially include **ascorbate**, proline and vitamin D or compds. thereof. The composition may also include N-acetylglucosamine and other compds. restoring and maintaining optimum biol. function of the vascular wall. A patient at risk of developing or with a pre-existing cardiovascular disease is treated by administering orally or parenterally a desired dosage of the composition on a daily basis.

ST **lysine** antiatherosclerotic **ascorbate** cardiovascular disease

IT Lipoproteins

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);
 BSU (Biological study, unclassified); BIOL (Biological study); OCCU

(Occurrence)

(Lp(a); **lysine** and **ascorbate** compds. for the treatment and prevention of cardiovascular diseases)

IT Antiarteriosclerotics

(antiatherosclerotics; **lysine** and **ascorbate** compds. for the treatment and prevention of cardiovascular diseases)

IT Drug delivery systems

(carriers; **lysine** and **ascorbate** compds. for the treatment and prevention of cardiovascular diseases)

IT Cardiovascular system

(disease; **lysine** and **ascorbate** compds. for the treatment and prevention of cardiovascular diseases)IT 50-81-7, **Ascorbic acid**, biological studies56-87-1, **Lysine**, biological studies 60-32-2, ϵ -Aminocaproic acid 67-97-0, Cholecalciferol 147-85-3,Proline, biological studies 657-26-1, **Lysine**dihydrochloride 657-27-2, **Lysine** hydrochloride

1197-18-8, Tranexamic acid 1406-16-2, Vitamin d 5408-52-6,

Lysine glutamate 7512-17-6, N-Acetylglucosamine 7776-34-3,Proline hydrochloride 12001-76-2, Vitamin B 18841-57-1, **Lysine**

orotate 29324-94-5 32511-63-0, 1,25-Dihydroxyvitamin d3 219942-03-7

219942-06-0 219942-08-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(lysine and ascorbate compds. for the treatment and prevention of cardiovascular diseases)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Eisai Kk; JP 60087221 A 1985 HCAPLUS

(2) Rath, M; US 5278189 A HCAPLUS

(3) Rath, M; US 5650418 A HCAPLUS

(4) Rath, M; WO 9119488 A HCAPLUS

(5) Rath, M; Journal of Applied Nutrition 1996, V48/3(68-78)

IT 50-81-7, **Ascorbic acid**, biological studies56-87-1, **Lysine**, biological studies 657-26-1,**Lysine** dihydrochloride 657-27-2, **Lysine** hydrochloride

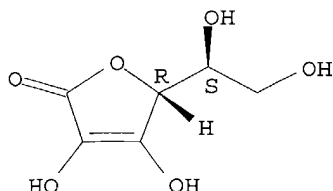
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(lysine and ascorbate compds. for the treatment and prevention of cardiovascular diseases)

RN 50-81-7 HCAPLUS

CN L-Ascorbic acid (8CI, 9CI) (CA INDEX NAME)

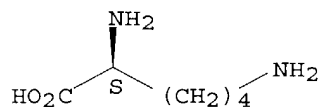
Absolute stereochemistry.



RN 56-87-1 HCAPLUS

CN L-Lysine (9CI) (CA INDEX NAME)

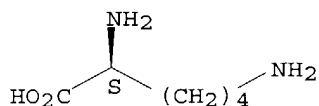
Absolute stereochemistry.



RN 657-26-1 HCAPLUS

CN L-Lysine, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

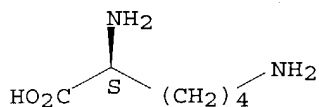


● 2 HCl

RN 657-27-2 HCAPLUS

CN L-Lysine, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L145 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:576691 HCAPLUS

DN 127:243272

ED Entered STN: 10 Sep 1997

TI Method and **composition** using purines and other compounds for inhibiting cellular irreversible changes due to stress

IN Miller, Guy; Lou, Lillian; Nakamura, John

PA Galileo Laboratories, Inc., USA

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-70

ICS C07H019-16; C07H019-20

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730713	A1	19970828	WO 1997-US2945	19970220 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,				

IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG

US 5801159	A	19980901	US 1996-607022	19960223 <--
CA 2247461	AA	19970828	CA 1997-2247461	19970220 <--
AU 9719749	A1	19970910	AU 1997-19749	19970220 <--
EP 935466	A1	19990818	EP 1997-907855	19970220 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

JP 2000506834	T2	20000606	JP 1997-530408	19970220 <--
NO 9803823	A	19981001	NO 1998-3823	19980820 <--

PRAI US 1996-607022 19960223 <--
WO 1997-US2945 19970220 <--

OS MARPAT 127:243272

AB **Formulations** of naturally occurring physiol. acceptable compds. and their derivs. are provided for treatment of cellular stress, particularly hypoxia. By administering the **formulations**, comprising for the most part purines, sugars, amino acids and physiol. acceptable derivs. thereof, by themselves or in **combination** with each other and with other compds., particularly electron acceptor compds., the time to irreversible cellular changes, particularly mortality, can be greatly extended.

ST purine sugar cytoprotectant cell stress; amino acid cytoprotectant cell stress; electron acceptor cytoprotectant cell stress

IT Diet
(and dietary supplement; purines and other compds. for inhibition of cellular irreversible changes due to stress)

IT Food
(and food bars; purines and other compds. for inhibition of cellular irreversible changes due to stress)

IT Carboxylic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxy; purines and other compds. for inhibition of cellular irreversible changes due to stress)

IT Stress, animal
(hypoxic; purines and other compds. for inhibition of cellular irreversible changes due to stress)

IT Carboxylic acids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxo; purines and other compds. for inhibition of cellular irreversible changes due to stress)

IT Animal tissue
Animal tissue culture
Beverages
Cytoprotective agents
Drug delivery systems
Electron acceptors
Glycolysis
Hypoxia, animal
Organ, animal
Stress, animal
Transplant and Transplantation
(purines and other compds. for inhibition of cellular irreversible changes due to stress)

IT Amino acids, biological studies
Dipeptides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(purines and other compds. for inhibition of cellular irreversible

changes due to stress)

IT Carbohydrates, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(reducing sugars; purines and other compds. for inhibition of cellular irreversible changes due to stress)

IT 50-44-2, 6-Mercaptopurine 50-89-5, Thymidine, biological studies
50-99-7, D-Glucose, biological studies **53-84-9**, NAD 56-40-6,
Glycine, biological studies 56-41-7, Alanine, biological studies
56-45-1, Serine, biological studies **56-65-5**, **Adenosine**
triphosphate, biological studies 56-85-9, Glutamine, biological
studies 56-86-0, L-Glutamic acid, biological studies **56-87-1**,
L-**Lysine**, biological studies 57-48-7, Fructose, biological
studies 58-55-9, Theophylline, biological studies 58-61-7, Adenosine,
biological studies 58-63-9, Inosine **58-64-0**, **Adenosine**
diphosphate, biological studies 59-23-4, Galactose, biological
studies 61-19-8, 5'-Adenylic acid, biological studies 61-73-4,
Methylene blue 63-91-2, L-Phenylalanine, biological studies 65-86-1,
Orotic acid 68-41-7, Cycloserine 71-30-7, Cytosine 73-03-0,
Cordycepin 73-22-3, Tryptophan, biological studies 74-79-3, Arginine,
biological studies 84-21-9, 3'-Adenosine monophosphate 85-31-4,
6-Mercaptoguanosine 107-35-7, Taurine 107-97-1, Sarcosine 118-00-3,
Guanosine, biological studies 120-73-0D, Purine, derivs.
127-17-3, **Pyruvic acid**, biological studies
131-99-7, 5'-Inosinic acid 146-80-5, Xanthosine 300-85-6
328-50-7, α -**Ketoglutaric acid**
488-69-7, Fructose-1,6-diphosphate 541-50-4, Acetoacetic acid,
biological studies 551-84-8, Xylulose 574-25-4, 6-Mercaptopurine
riboside 598-41-4, Glycine amide 600-18-0, α -Ketobutyric acid
616-34-2, Glycine methyl ester 643-13-0, Fructose-6-phosphate
653-63-4, 2'-Deoxyadenosine monophosphate 820-11-1, 3-Phosphoglyceric
acid 890-38-0, Deoxyinosine 892-48-8, 5'-Chloro-5'-deoxyadenosine
902-04-5 958-09-8, Deoxyadenosine 961-07-9, Deoxyguanosine
1053-73-2, 3',5'-**Adenosine diphosphate** 1113-60-6,
 β -**Hydroxypyruvic acid** 1118-68-9, N,N-Dimethylglycine
2002-28-0, Ribulose-1,5-diphosphate 2004-07-1, 2-Amino-6-chloropurine
riboside 2140-73-0, 1-Methylinosine 2140-77-4 2140-79-6,
2'-O-Methyladenosine 2239-64-7 2304-12-3, Adenosine 5'-monosulfate
2457-80-9, 5'-Deoxy-5'-methylthioadenosine 3393-18-8 3458-28-4,
Mannose 3805-37-6, 2',5'-**Adenosine diphosphate**
4431-00-9, Aurintricarboxylic acid 4546-70-7 4754-39-6,
5'-Deoxyadenosine 5399-87-1, 6-Chloropurine riboside 5556-48-9,
Ribulose 5682-25-7, α -Adenosine 6915-15-7, **Malic acid**
10065-72-2, Alanine methyl ester 10139-18-1, Glucose-1,6-diphosphate
14365-44-7, 5'-Amino-5'-deoxyadenosine 20245-33-4, 7-Methylinosine
20762-30-5, Adenosine 5'-diphosphoribose 24280-93-1, Mycophenolic acid
24386-93-4, 5-Iodotubercidin 27025-41-8, Oxidized glutathione
29884-64-8, Threose 29886-19-9, 2', 3'-Di-O-acetyladenosine
32266-35-6, Dibutyryl cyclic GMP 35899-54-8 38048-32-7,
S-4-Nitrobenzyl-6-thioinosine 41552-82-3, N6-Cyclopentyladenosine
51350-19-7, erythro-9-(2-Hydroxy-3-nonyl)adenine 53296-10-9,
2-Phenylaminoadenosine 56964-73-9 79082-92-1, Fructose-2,6-diphosphate
102029-71-0, Adenosine 5'-**succinate** 195503-37-8
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(purines and other compds. for inhibition of cellular irreversible
changes due to stress)

IT **53-84-9**, NAD **56-65-5**, **Adenosine**
triphosphate, biological studies **56-87-1**, L-
Lysine, biological studies **58-64-0**, **Adenosine**
diphosphate, biological studies **127-17-3**,

Pyruvic acid, biological studies 328-50-7,

α -Ketoglutaric acid

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL

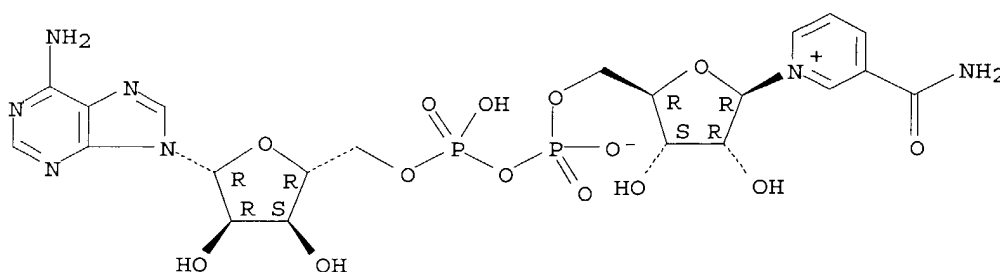
(Biological study); USES (Uses)

(purines and other compds. for inhibition of cellular irreversible changes due to stress)

RN 53-84-9 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate), P' \rightarrow 5'-ester with
3-(aminocarbonyl)-1- β -D-ribofuranosylpyridinium, inner salt (9CI)
(CA INDEX NAME)

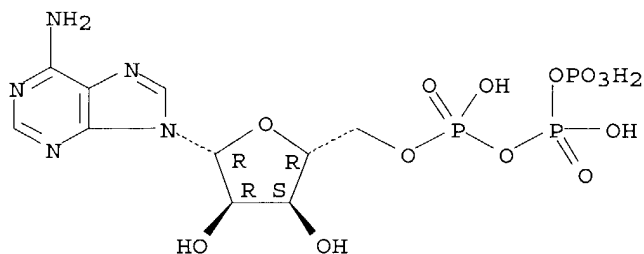
Absolute stereochemistry.



RN 56-65-5 HCAPLUS

CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

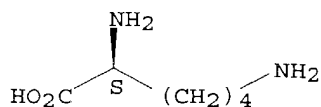
Absolute stereochemistry.



RN 56-87-1 HCAPLUS

CN L-Lysine (9CI) (CA INDEX NAME)

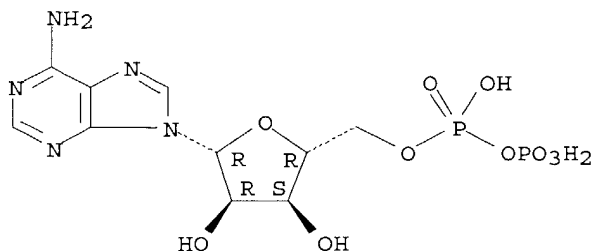
Absolute stereochemistry.



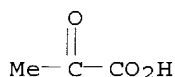
RN 58-64-0 HCAPLUS

CN Adenosine 5'-(trihydrogen diphosphate) (9CI) (CA INDEX NAME)

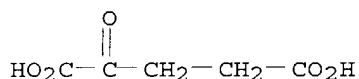
Absolute stereochemistry.



RN 127-17-3 HCAPLUS
 CN Propanoic acid, 2-oxo- (9CI) (CA INDEX NAME)



RN 328-50-7 HCAPLUS
 CN Pentanedioic acid, 2-oxo- (9CI) (CA INDEX NAME)



L145 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1997:132781 HCAPLUS

DN 126:139892

ED Entered STN: 28 Feb 1997

TI Processes, compounds, and **compositions** for augmented ATP production, and therapeutic and other uses

IN Fahy, Gregory M.

PA Organ, Inc., USA; Life Resuscitation Technologies, Inc.

SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-70

ICS A61K031-115

CC 1-10 (**Pharmacology**)

Section cross-reference(s): 9, 13, 18, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9640167	A1	19961219	WO 1996-US10255	19960607 <--
	W: AU, CA, CN, JP, KR, SG				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5707971	A	19980113	US 1995-476035	19950607 <--
	CA 2223327	AA	19961219	CA 1996-2223327	19960607 <--
	AU 9661754	A1	19961230	AU 1996-61754	19960607 <--
	EP 831853	A1	19980401	EP 1996-919403	19960607 <--
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, IE				
PRAI	US 1995-476035			19950607 <--	
	WO 1996-US10255			19960607 <--	
AB	Delivery of fuel and cofactors augments ATP production in cells, and mitigates damages in ischemic or metabolically impaired tissues. The processes may				

be particularly effective in acute or chronic ischemic conditions, for reversing anesthesia, for treating diabetes, for producing or preventing coma due to lack of fuel of ATP, for reversing processes of aging, as dietary supplements, as performance enhancers (e.g. for sports), for tissue transplantation and other surgery, and for cold storage or cryopreservation of tissues such as organs. Compds. disclosed include NAD⁺, CoA, **acetyl CoA**, glyceraldehyde-3-phosphate, etc.

- ST ATP augmentation ischemia diabetes anesthesia reversal; diet supplement pharmaceutical ATP augmentation; aging athletic performance enhancer ATP augmentation; transplantation surgery cryopreservation ATP augmentation; oxidative metab impairment ATP augmentation; NAD CoA **acetyl CoA** ATP augmentation; glyceraldehyde phosphate ATP augmentation
- IT Antidiabetic agents
 - Blood products
 - Cytoprotective agents
 - Drug delivery systems
 - Exercise
 - Hypothermia
 - Hypoxia, animal
 - Ischemia
 - Surgery
 - Transplant and Transplantation
 - (ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Exercise
 - (athletic performance; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Drug delivery systems
 - (controlled-release; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Organ preservation
 - (cryopreservation; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Hypoglycemia
 - (death associated with; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Coma
 - (diabetic; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Death
 - (hypoglycemia-associated; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Drug delivery systems
 - (oral; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT **Metabolism**
 - (oxidative, tissue with impaired; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Aging, animal
 - (reversal of processes of; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Anesthesia
 - (reversal; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Kidney
 - (slices, cold storage; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT Diet
 - (supplements; ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)
- IT **53-84-9, NAD 72-89-9, Acetyl CoA**
 79-43-6, Dichloroacetic acid, biological studies 85-61-0, CoA,

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ATP augmentation processes, compds., and compns., and therapeutic and other uses)

IT 7782-44-7, Oxygen, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (deficit; ATP augmentation processes, compds., and **compns.**,
 and therapeutic and other uses)

IT 53-84-9, NAD 72-89-9, Acetyl CoA
127-17-3, biological studies 541-15-1, Carnitine

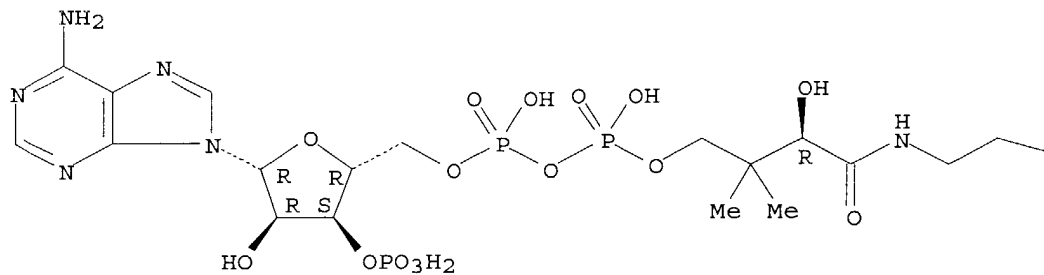
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (ATP augmentation processes, compds., and compns., and therapeutic and other uses)

CN Adenosine 5'-(trihydrogen diphosphate), P'-5'-ester with
3-(aminocarbonyl)-1-β-D-ribofuranosylpyridinium, inner salt (9CI)
(CA INDEX NAME)

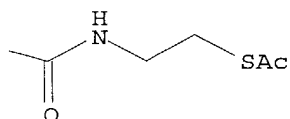
CN	Coenzyme A, S-acetate (6CI, 8CI, 9CI)	(CA INDEX NAME)
----	---------------------------------------	-----------------

Absolute stereochemistry.

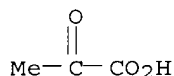
PAGE 1-A



PAGE 1-B

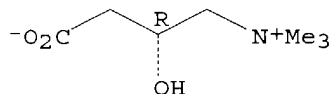


RN 127-17-3 HCAPLUS
 CN Propanoic acid, 2-oxo- (9CI) (CA INDEX NAME)



RN 541-15-1 HCAPLUS
 CN 1-Propanaminium, 3-carboxy-2-hydroxy-N,N,N-trimethyl-, inner salt, (2R)- (9CI) (CA INDEX NAME)

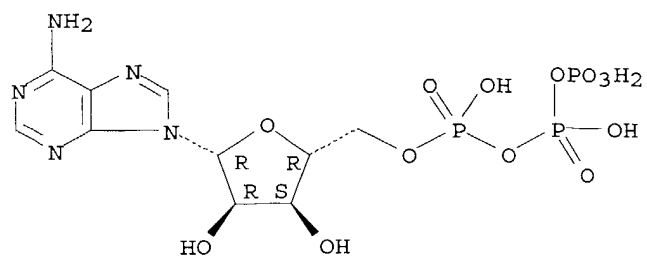
Absolute stereochemistry. Rotation (-).



IT 56-65-5, biological studies
 RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (ATP augmentation processes, compds., and **compns.**, and therapeutic and other uses)

RN 56-65-5 HCAPLUS
 CN Adenosine 5'-(tetrahydrogen triphosphate) (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



=>